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Public Health

The order in this section is:—**General; Vital Statistics; Epidemiology; Maternal and Child Health; Health of Students, Nurses and Hospital Staffs; Health of Old Persons and the Chronically Ill; Chronic Cardio-Respiratory Diseases; Chronic Rheumatism; Cancer; Miscellaneous Diseases; Dental Health; Mental Health.**

GENERAL

MINISTRY OF HEALTH. **Report of the Ministry of Health for the Year 1959. Part II. On the State of the Public Health being the Annual Report of the Chief Medical Officer** [CHARLES, J. A.]. Cmnd. 1207, pp. vii + 292, 1 fig., 1 graph and 3 diagrams. 1960. London: H.M. Stationery Office. [13s.]

This is the last annual report to appear from the erudite pen of Sir John Charles, who has recently retired, and it is a fitting testimonial that it records advances in so many directions.

[The report for 1958 was reviewed in this *Bulletin*, 1960, v. 35, 329.]

The special chapters in the 1958 report on the common respiratory diseases and on medical rehabilitation are replaced by new ones on the control of infection in hospitals, services available to the elderly and recent developments in urology.

The year 1959 was memorable for its fine summer weather: the best since 1911.

The population is now 45,386,000; an increase of 277,000 during the year, of which immigration accounted for 48,000. It is estimated that by 1979 the population will be 49,230,000.

The birth rate was 16·5 and the death rate 11·6 per 1,000 population: 41% of male deaths at ages 15–24 were due to road traffic accidents and half the total deaths at all ages to diseases of the heart and circulatory system. The rate of infant mortality was 22·2 per 1,000 live births and the neonatal death rate 15·9; neither of which has ever been lower in England and Wales. The still-birth was 20·8 per 1,000 total births and is, also, a low record. The perinatal mortality was 34·1. The maternal mortality was 0·38 per 1,000 total births and includes post-abortion deaths.

For the first time since notification began there was no death from diphtheria but 102 cases were notified compared with 37 and 80 in the two previous years. There were 48,000 notifications of scarlet fever but only one death: 539,524 of measles with 98 deaths (one-fifth complicated by encephalitis): 33,252 of whooping cough with 25 deaths (11 at under 6 months): 1,028 of poliomyelitis with 87 deaths, the incidence being the lowest since 1946. The virus most frequently isolated was Type I. There is a sub-chapter on vaccination against poliomyelitis summarized by the remark that there is "again a record of magnificent achievement by the local health authorities". Influenza caused 7,862 deaths, the highest since 1951 and pneumonia 27,340 the highest since 1940. There is an appraisal of the value of influenza vaccines.

There was another outbreak of benign myalgic encephalomyelitis: this time at a teachers' training college in Newcastle. There were no serious after effects. The incidence of gonorrhoea shows a "spectacular" increase.

In a reference to the best place for an ailing child it is stated that it is his home "and his best nurse his mother".

The Miners' Rehabilitation Service returned 72% of its clients to their pre-accident work and another 22% to lighter work in the mines: in only 0·3% was there a failure to provide adequate resettlement.

Matters which receive full treatment in the chapter on epidemiology are anthrax, undulant fever, lepropsy, Q fever, the complications of vaccination against smallpox, poliomyelitis in Southampton (128 cases and 5 deaths), an outbreak of diphtheria in North London and in that on the Laboratory Services sewage contamination of bathing beaches and the detection of typhoid carriers among waterworks employees. A disinfection reference unit has been set up.

Tuberculosis caused 3,854 deaths which is a rate of 85 per million population: all forms are 14% lower than in 1958. The notifications numbered 27,100 which include those found by mass miniature radiography: 317,043 school children were vaccinated with BCG.

There are valuable chapters on the rheumatic diseases and on the cancers. The cancer death rates per million population were males 2,366 and females 1,929; among the males, the stomach was the site in 15% and the respiratory system in 37%: among females, 14% stomach and 19% breast. There is a full description of recent developments in radiotherapy.

Mental health receives much attention. There are 15,000 fewer patients in mental hospitals than there were in 1955, the peak year. "There is no doubt whatever

that the practice of psychiatry has undergone a revolution in the past ten years and that active and effective treatment has been the primary cause." The number of consultant psychiatrists has increased from 405 in 1949 to 648 in 1959 and of all the senior registrars in the hospital service one-fifth are training in psychiatry. Statistical enquiries have been proceeding for some years and the findings are that almost three-quarters of those admitted to admission wards are discharged within 3 months: the main wards contain 80% of the patients but the majority are able to leave within 2 years and 4% of all discharges are from those who have been in the hospital for 5 or more years. "The aim of a modern psychiatric hospital should be to be left with no 'chronic' patients, young or old."

The section on "Rehabilitation in Mental Disorder" is of outstanding value and should be studied by all concerned with the care of mental patients.

The chapter on "General Public Health" contains an able essay on the functions of a modern health department. That on "Maternal and Child Care" discusses in detail premature births, phenylketonuria, the welfare of children in hospital, changing trends in maternity and child welfare centres and the guidance of parents of handicapped children.

The dental health service is still handicapped by shortage of dentists: one local authority has appointed a dental health education officer.

In the chapter on the elderly it is stated that 96% of old people live at home and that most are well and active but 10% are house- or bed-bound by infirmity. The help which can be given by suitable housing, the domiciliary services including chiropody, the welfare services (more than 1,100 "small homes" have been opened since 1945) and hospitals (there are 95 geriatric units) is described.

The new chapter on urology describes recent advances in the diagnosis and treatment of diseases and abnormalities of the genito-urinary tract. In the hospital service there are 1,218 beds allocated to this specialty.

The appendix contains 29 pages of tables. There is no index which is a pity.

The reading of this report is an excellent refresher course for all engaged in any branch of the public medical service. *Allen Daley*

MATERNAL AND CHILD HEALTH

NORTHERN IRELAND, GOVT. OF. **Operation of Social Services in relation to Child Welfare. Report by the Northern Ireland Child Welfare Council** [HAUGHTON, M. A. F. E., Chairman]. 45 pp. 1960. Belfast: H. M. Stationery Office. [3s.]

This study, carried out by a study group of the Northern Ireland Child Welfare Council, enumerates and analyses the causes which led to a child coming into the care of a welfare authority or voluntary organization. All the registered voluntary homes and welfare authorities supplied details of all the children who were in their care on 31st May, 1957, and 30th June, 1957, respectively. Details of 1,899 children were collected. Additional information was collected by interviewing the children's officers of the welfare authorities.

Significant differences were found between the reasons that children came into the care of welfare authorities as compared with those coming into the care of voluntary homes. Nearly 23% of the children in the care of the welfare authorities had been committed to their care by the courts, no children in the voluntary homes had been so committed; 18% of the children were in the care of the authorities because of illness of the mother, 13% because of the death of or desertion by one or other parent and 12% because they had been abandoned or had no parent or guardian. Illegitimacy associated with the inability of the mother to provide for the child was the reason for nearly 14% of the children being in the care of the welfare authorities, but in the voluntary homes, illegitimacy associated with inability of the mother accounted for the admission of 52% of the children, while death of or desertion by one or other parent accounted for 17%, and illness of the mother 8%. Neglect, moral danger and unsuitable foster homes formed only a small percentage but were more common among the children in the care of the welfare authorities.

This study showed that on the date of the survey 4 out of every 1,000 children under the age of 18 years were in care; about 60% of the children in care being with the welfare authorities and 40% with the voluntary homes. The welfare authorities provided for all children committed by the courts, and for the greater number of children whose mothers were ill, who were orphaned or abandoned or who were in moral danger or neglected. The voluntary homes were providing for homeless, illegitimate children and children whose parents were separated or divorced. With the emphasis on and a strong tradition of boarding-out in Northern Ireland, the welfare authorities were found to be increasingly providing for short-stay cases, and using the voluntary homes where they considered that institutional care was more suitable than boarding-out.

In general, it was found that the different welfare authorities adopted similar policies in taking children into care, but significant variations were found in the practices of the 6 largest voluntary homes. These differences, in part, reflected the policies of the homes concerned. The pattern of age distribution of the children was broadly similar in both types of care. Parents or relatives kept contact with 65% of the legitimate children and 38% of the illegitimate children in the care of the welfare authorities; the figures for the children in the voluntary homes being 87% and 55% respectively. These differences are associated in part with the differences in the reasons for coming into care.

The Report points out that the total number in care was lower than the comparable figures for England and Wales and Scotland; but believes that, in general, the authorities were providing adequately for all children in

need of care. [No factual evidence is given in support of this belief.] The study group recommends, among other matters, further study of the problem of children of unmarried mothers, continued care in the choice of foster-homes, the maintenance of a central register of all children in the care of both the voluntary and statutory bodies, that voluntary homes be encouraged and helped to employ an adequate field-staff and that the whole question of after-care by both bodies shall be studied afresh.

This is a valuable study giving much new information, concisely discussed and tabulated in a series of appendices to the main report. *M. D. Warren*

HOLLINGSWORTH, M. J. **The Birth Weights of African and European Babies born in Ghana.** *West African Med. J.* 1960, Dec., v. 9 (n.s.), No. 6, 256–9.

MAYON-WHITE, R. M. **Winter Ailments of the Infant and Young Child.** *Practitioner.* 1960, Dec., v. 185, No. 1110, 743–8. [11 refs.]

An infant's hands and feet become blue and swollen when cold, but are easily re-warmed. Schoolchildren tend more to suffer from chilblains, especially in raw damp weather, above freezing point. Damp Wellington boots are conducive to this; dry socks and shoes for school wear are advised. Infants suffer easily from hypothermia. Cold injury probably kills more infants today than over-lying ever did.

Acute laryngeal obstruction is a major hazard in infants. Congenital laryngeal stridor is usually associated with micrognathia and hypoplastic larynx, combined with infection. Tracheostomy must be avoided, if possible, as it may become a permanent necessity. Croup is now usually non-diphtheritic in Britain. Admission to hospital in such cases should never be refused if the practitioner thinks it necessary. The child who is in urgent need of a tracheostomy shows little cyanosis (at first) but air hunger sufficient to make him thrash about in his cot.

Differentiation of lower respiratory tract infections is important between acute epidemic bronchiolitis and pneumonia in infancy. A chest radiograph is usually helpful. Epidemic bronchiolitis does not respond to antibiotics, except in the stage of bacterial superinfection.

Poisoning by phenobarbitone, aspirin, and ferrous sulphate is relatively common at all seasons, but kerosene swallowing is a winter phenomenon.

Much care and discrimination are necessary by house physicians in winter in determining admissions of sick children, especially infants, to hospital. If the family doctor "doesn't like the look of the child", that should be a grave warning as to the possible consequences of refusal of admission. *H. Stanley Banks*

COPITHORNE, R. E. C. & PALMER, W. T. **A Survey of Pupils from Schools for the Delicate in London.** *Med. Officer.* 1960, Nov. 25, v. 104, No. 22, 323–5.

This paper is from the public health department of the London County Council and is a survey of the 564 children who left the Council's special schools for the delicate during 1958.

These schools were started about 50 years ago and are commonly known as "open air" schools [this *Bulletin*, 1959, v. 34, 307]. Some are boarding schools but this paper deals only with the 12 day schools which have a combined school roll of 1,486, 908 boys and 578 girls. Of the 564 who left in 1958, 353 were boys and 211 girls. The total school rolls of London for all types of school contain 430,000 names.

An analysis was made by Dr. Copithorne of the reasons why the 564 were admitted: by far the largest group was "respiratory" namely 66·3%; 32·9% of the total were suffering from asthma, 13·5% from bronchitis, 4·1% bronchiectasis, and 9·6% primary tuberculosis. In addition, 18·4% were marked simply "debility" and 2·8% were contacts of tuberculosis; the rest included a wide range of miscellaneous conditions. The reasons for admission per 1,000 on the total school rolls were asthma, 0·95; bronchitis, 0·39; bronchiectasis, 0·12; primary tuberculosis, 0·28; other respiratory, 0·18; "Nutrition" group, 0·66; all other conditions, 0·31.

The age at admission ranged from 4 to 14 years and the duration of stay up to 10 years though normally it was between 1 year and 2.

The reasons for discharge were special education completed, 61·6%; transferred elsewhere for special education, 28·8%; parents removed, 7·8%; parents requested discharge, 1·8%.

Allowing for transfers between special schools owing to alterations in the "catchment areas", in 75% of the discharges special education was completed; in another 14% it was known to be continuing and the latter applied to each of the medical reasons for admission.

The future of the schools is discussed in the context that originally all these schools had at least one side completely open to the elements but now they are all enclosable and differ little architecturally from recently built ordinary schools; the real difference now from ordinary schools is the provision of extra meals and milk, bed rest periods, transport to and from school, an extra year at school for those at the end of their school life and "open air".

The authors conclude "It is suggested that the 'open-air regime' will continue to be of benefit to some three per 1,000 of the total school rolls for some years to come"; "the child [suitable for admission] is most likely to be ready for discharge in about five terms (somewhat longer for asthmatics)". *Allen Daley*

HEALTH OF OLD PERSONS AND THE CHRONICALLY ILL

EXTON-SMITH, A. N. **Winter Ailments in the Elderly.** *Practitioner.* 1960, Dec., v. 185, No. 1110, 735–42, 1 fig. [14 refs.]

Admissions to hospitals in Britain are much more common in the elderly in winter than in summer, especially because of respiratory disorders (7-fold), heart disease (3-fold) and cerebral catastrophe (2·5-fold). Respiratory disease often reacts on the cardio-vascular system and *vice versa*. The impairment of homoeostatic mechanisms in the ageing body can bring about severe hypothermia with very low rectal temperature, under conditions of unintentional exposure, such as an accident in the home or elsewhere. The treatment of such degrees of hypothermia is not by moderate surface re-warming (which dilates surface vessels and brings an increased volume of cold blood into the viscera), nor by rapid heating as in a hot bath (which by sudden peripheral dilatation may bring about a fatal fall in blood pressure), but by slow raising of the body temperature at a room temperature of about 70°F. by the patient's own metabolism. During this process antibiotics may be given as a prophylactic against respiratory infection.

H. Stanley Banks

CANCER

STOCKS, P. **On the Relations between Atmospheric Pollution in Urban and Rural Localities and Mortality from Cancer, Bronchitis and Pneumonia, with particular reference to 3:4 Benzopyrene, Beryllium, Molybdenum, Vanadium and Arsenic.** *Brit. J. Cancer.* 1960, Sept., v. 14, No. 3, 397–418. [14 refs.]

Filters to measure the smoke concentration and the different elements contained within it were installed in 26 localities in Northern England and Wales. The resulting measurements (for 1957 and 1958) have been correlated with the recorded death rates (standardized mortality ratios) from different forms of cancer, bronchitis and pneumonia (in 1950–53 or 1950–54). When social factors are kept constant, by means of partial correlation technique, there is an appreciable relationship between the total smoke concentration and mortality from cancer of the lung, bronchitis and pneumonia but not with mortality from cancer of the stomach or breast. With cancer of the lung and bronchitis the evidence points to 3:4 benzopyrene as the hydrocarbon specially concerned while with pneumonia there is a residual association in males with 1:12 benzoperylene and in females with fluoranthene. With the trace elements measured there appear to be significant correlations between cancer of the lung and the amounts in air of beryllium, molybdenum and arsenic, and weaker associations with zinc and vanadium. For bronchitis molybdenum appears to be the important element in both sexes whilst in men beryllium, arsenic, vanadium and zinc may also be concerned. For pneumonia beryllium emerges as the important element in both sexes with vanadium also concerned in men. With other forms of cancer in men beryllium, molybdenum and vanadium show associations.

Published data on the amounts of smoke and atmospheric deposit in urban areas of England and Wales can also be related to variations in mortality [this *Bulletin*, 1959, v. 34, 1144]. Such correlations have been computed for groups of county boroughs, for administrative areas in Lancashire and the West Riding of Yorkshire, and for Greater London. The amount of atmospheric deposit is significantly, though not very highly, correlated with mortality from cancer of the lung, cancer of the stomach, bronchitis and pneumonia. The amount of smoke appears to be slightly correlated with the mortality from cancer of the lung, bronchitis and pneumonia (coefficients between 0·2 and 0·4). Cancers of the stomach and intestine also show significant association in the county boroughs and cancer in males of sites other than lung and stomach are similarly related in the other groups of areas.

A. Bradford Hill

STASZEWSKI, J. **Smoking and Cancer in Poland.** *Brit. J. Cancer.* 1960, Sept., v. 14, No. 3, 419–36. [10 refs.]

The consumption of tobacco in Poland rose sharply after the second world war. The average per head of the population was about 550 gm. per annum in the 1930's and had risen to nearly 1500 gm. by 1957. Underlying this change is a great reduction in the use of pipe tobacco and a great increase in the use of cigarettes. In recent years there is evidence of a considerable increase in mortality from cancer of the respiratory organs.

Detailed evidence on smoking habits and other personal characteristics was obtained from 281 patients with cancer of the lung (260 men and 21 women) and compared with similar data from other patients seen at the Institute of Oncology (mainly with forms of cancer not likely to be related to smoking, such as the genital organs, skin, large intestine and rectum). The two groups were alike in average age, proportion resident in towns and history of pneumonia, but differed very considerably in their smoking habits and histories. For example, the mean index of past smoking (daily amount smoked, in grammes, multiplied by duration of smoking, in years) was 612 for men with cancer of the lung and 406 for the control group. The corresponding figures for women were 99 and 12. Of the smoking men with cancer of the lung 92% were classified as heavy smokers compared with 59% of the controls. 96% inhaled compared with

81% of the controls. 86% smoked only cigarettes compared with 73% of the controls. These differences were rather less marked in 20 cases of adenocarcinoma. No connexion was found between cancer of the lung and blood groups. It is calculated that a smoker has about a 10-fold greater chance of lung cancer than a non-smoker.

Similar data were collected for men suffering from cancers of the lip, oral cavity, tonsils and larynx and these can be contrasted with the same controls and with a further group of 200 farmers with cancer of the skin. In each case some association with smoking habits is observed but at a generally lower level than that noted with cancer of the lung. *A. Bradford Hill*

PAYET, M., CAMAIN, R., SANKALÉ, M. & PÈNE, P. Les hémopathies malignes chez l'Africain (à propos de cent cas). **[Leukaemias and Malignant Growths of Blood-forming Tissues in Africans]** *Bull. Soc. Méd. Afrique Noire Langue Francaise.* Dakar. 1960, v. 5, No 3, 205–22. [41 refs.]

Of 100 cases studied during 10 years in Dakar under the above heading, there were 28 of leukaemia, 24 of of Hodgkin's disease, 10 of plasmocytoma, and 42 of sarcoma [4 of this total of 104 had both leukaemia and sarcoma] arising from various parts of the lymphoreticular tissue. This does not represent an exact relative incidence, since there were many insufficiently studied patients in the same period, who were not included. However, the general pattern corresponds fairly closely with that reported from Ghana, Nigeria, Uganda, the Congo, and Mozambique, and emphasizes the frequency of sarcoma of haemopoietic organs, especially the spleen, liver, and lymph nodes. The rapid progression and wide diffusion of such sarcomas is noted. The other diseases mentioned occur about as often in Senegalese as in whites, but acute leukaemia (3 cases) is noticeably rarer, as DAVIES (*Cancer in Africa.* In *Modern Trends in Pathology,* Ed. D. H. Collins, 1959; London, Butterworth) found in Uganda. *Alan B. Raper*

PELOUX, Y. Le cancer en Nouvelle-Calédonie. Statistique anatomo-pathologique des années 1949 à 1959. **[Cancer in New Caledonia, 1949–59]** *Méd. Trop.* Marseilles. 1960, Sept.–Oct., v. 20, No. 5, 613–17.

This is a statistical and pathological account of malignant disease occurring in New Caledonia in the period 1949–59. There were 500 cases investigated at the Institut Pasteur in Noumea, which is a number considered to give a good picture of the cancer incidence of the territory. The population in this period ranged from 64,000 to 71,000 persons. In 1959 there were 26,500 Europeans, 37,500 Melanesians, 4,500 Asians and 2,700 Polynesians. The annual cancer incidence is recorded in a table. Of the total of 500 cases 314 were in Europeans, 130 in Melanesians, 35 in Asians, and 21 in Polynesians. The type and site of the tumours are set out in this table.

Among the Europeans the cancer picture was practically the same as in the mother country except for the greater frequency of cutaneous cancer. In Melanesians the overall incidence is less than in Europeans and the skin is much less frequently involved but in the female there was a high proportion of uterine and mammary cancer. A particularly high incidence of cancer of the liver was noted in the Melanesians—12 cases among the total of 130 cancers. *M. E. Delafield*

Sanitation

The order in this section is:—**General; Water and Swimming Baths; Sewage, Trade Waste and Refuse Disposal; Housing; Infestation; Atmospheric Pollution Port, Ship and Aviation Hygiene.**

WATER AND SWIMMING BATHS

ANDÉN, T., KJELLANDER, J. & NYGREN, B. Vatten från Göta älv som orsak till enteritepidemi på fartyg. **[Water from Gothenburg as a cause of *Salmonella-Shigella* Infection in a Ship]** *Nordisk Hyg. Tidskr.* 1960, v. 41, Nos. 11/12, 269–271.

The English summary appended to the paper is as follows:—

"An epidemic of 25 cases of salmonellosis and shigellosis is described. The cases occurred on board a ship in the harbour of Gothenburg after a mistake of filling drinking water tanks with the highly polluted river water. It is suggested that the water intakes on board should be painted in different colours to prevent further mistakes."

J. AMER. WATER WORKS ASS. 1960, Dec., v. 52, No. 12, 1513–20, 4 figs. **Status of Fluoridation in the United States and Canada, 1959. A Report of Task Group 2620P** [MAIER, F. J., Chairman].

BARTLEY, Clara H. & SLANETZ, L. W. **Types and Sanitary Significance of Fecal Streptococci isolated from Feces, Sewage and Water.** *Amer. J. Pub. Health.* 1960, Oct., v. 50, No. 10, 1545–52. [12 refs.]

Faecal streptococci were isolated from various animal faeces, water and sewage samples by membrane filtration and incubation on Slanetz and Bartley M-enterococcus agar [this *Bulletin,* 1958, v. 33, 495], presumably

with incubation at 35° or 37°C. The Sherman tests were carried out on all strains isolated, together with a number of other tests. All varieties and biotypes of *Strep. faecalis* isolated from human faeces failed to ferment raffinose and typical *Strep. faecalis* was not isolated from any animal except in one instance from a dog. The raffinose-fermenting tellurite-resistant streptococci appeared to be of animal origin, particularly from cows and sheep. Tellurite sensitive organisms resembling *Strep. inulinaceus* outnumbered *Strep. faecalis* and *Strep. faecium* in fresh human samples but the reverse was true for sewage and sewage polluted water. Furthermore there was greater variation in characteristics of strains isolated from sewage than from those from faeces.

Viability studies on pure cultures contained in dialyzing bags suspended in natural waters at about 20°C. revealed decreases of 25 to 75% in the first 24 hours with only small numbers remaining after 7 days. Samples of water stored at 8°C. showed little change in numbers in 48 hours but numbers decreased in 24 hours at 26°C.

E. Windle Taylor

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

Del Vecchio, V., Bellante, E., D'Arca Simonetti, A. & De Martiis, G. Lo stato di inquinamento dell 'acqua marina nella zona costiera di S. Felice Circeo. 1ª nota, relativa alla stagione estiva 1959. [**The Existing State of Contamination of the Sea Water off the Coast of S. Felice Circeo. 1st Report relating to the Summer of 1959**] *Igiene e San. Pubblica.* Rome. 1960, July–Aug., v. 16, Nos. 7/8, 397–430, 10 figs. (4 folding). [53 refs.]

The authors, the senior of whom is the Director of the G. Sanarelli Institute of Hygiene of the University of Rome and one of the best-known experts in Public Health in Italy, give an account of tests to estimate the extent of contamination of the sea water off the coast of a little town S. Felice Circeo which lies about 100 km. from Rome. Through its excellent beaches and the beauty of the country-side (a national park practically adjoins it) it has become increasingly popular; the normal population of the town (3,500 in 1953) had in that year in the summer over 5,000 additional inhabitants. The sewage disposal arrangements are totally inadequate and unsatisfactory and discharge is into the sea by pipes or open sewers, in many instances directly on to the beach above water level. However the Cassa per Il Mezzogiorno (Southern Italy Development Fund) is now providing the money for a complete reconstruction of the sewers and technical aid is being given by the National Civil Engineer's Department, hence this report is a preliminary one designed to get some idea of the existing contamination of the sea water off the beaches of which there are really two, one immediately below the populous part of the town which is naturally very crowded in summer, the other rather over 2 km. away which is not. As a matter of historical interest a former ship canal used by the ancient Romans to allow their galleys to reach Rome without having to navigate round the feared cape Circeo which lies to the west of the town, now, alas, functions as an open sewer! Sampling took place from July to October 1959 from 107 points at a depth of as far as possible 50 cm., and over a distance of about 4 km., and on either side of the various outfalls. The samples of 200 cc. each were then examined by "Standard Methods" for total organisms, at 37°C., and *Escherichia coli* by IMViC with estimation of the most probable number. In addition salinity (chlorides) was estimated to see if there was any material dilution through the outfalls.

The results from the 107 sampling points are set out in a table, and 2 maps and several graphs are drawn showing log total organisms, and *coli*. The authors point out that all gradations occur between water that is definitely contaminated and that which is doubtful, while our knowledge of any correlation between disease and the contamination of sea-water off bathing beaches is scanty.

As might be expected the log contour maps demonstrate emphatically the extent of contamination near the main outfalls; the log 2 *coli* extends in many places to about 100 m. seaward [even more off the largest outfall]; the log 4 contour for total organisms extends even from the furthest end of the most unfrequented beach, and its log 5 extends at least 500m. seaward from the largest outfall. From the maps there appears however to be some drift from North East to South West especially from the largest outfall as from the scale log 2 *coli* is found nearly 1 km. from this outfall, and the same obtains for log 5 total organisms.

The authors point out that the log total organisms contour is much more regular than that for *coli* and so is less indicative of the outfalls; there is practically no correlation between salinity and bacterial content; *coli* did not fall below log 2 for at least 90 m. from the beach below the town. They conclude therefore that there is extensive existing contamination of the seawater off the main beach and that it cannot be regarded as safe for bathing for at least 90 m. seaward.

[A point of interest is that of the 16 samples taken in October (when presumably all the "temporary residents" had departed), some still showed at certain sampling points a considerable degree of contamination even 100 m. or more from one of the outfalls.]

W. K. Dunscombe

Bhaskaran, T. R., Lahiri, M. N. & Ghose Roy, B. K. **Effect of Sewage Treatment Processes on Survival of Tubercle Bacilli.** *Indian J. Med. Res.* 1960, Nov., v. 48, No. 6, 790–96, 2 figs.

The work described in this paper was undertaken because the data on the occurrence of tubercle bacilli in the wastes from sanatoria and slaughter-houses in India are scanty and the efficiency of sewage treatment plants in removing these organisms is also not known.

The investigations were carried out on waste waters

from 2 sanatoria and 1 slaughter house near Calcutta and also at the sewage treatment plants attached to the sanatoria. There is an account of the methods employed for the bacteriological examination of the wastes and in animal inoculation experiments. The main results were that (1) viable tubercle bacilli were demonstrated in about 95% of the 94 samples of raw sewage from the 2 sanatoria, (2) sewage treatment by sedimentation, septic tank and bio-filtration was not effective in removing the organisms to any great extent, and (3) tubercle bacilli were isolated from 7 of 9 samples of digested and dried as well as fresh sewage sludge.

The animal experiments did not demonstrate so high a proportion of positives as did the culture technique studies.

No tubercle bacilli were demonstrated in 33 samples taken at different times from the waste water from the slaughter house.

A pilot plant has been designed to test the efficacy of chlorine disinfection of sanatorium sewage effluent following laboratory experiments which have shown that a high dose of chlorine sufficient to leave a residual of 1·0 p.p.m. at the end of half an hour is adequate for the purpose. Sludge samples can be rendered safe only by heat treatment of 60°C. held for at least 30 minutes.

M. E. Delafield

ATMOSPHERIC POLLUTION

SHABAD, L. M. & DIKUN, P. P. **Atmospheric Pollution by the Carcinogenic Substance 3, 4-Benzpyrene.** [Translated from Russian by B. HAIGH.] Pts. A & B. 353 and 359 Xerographed pp., numerous figs. [Numerous refs.] 1960, December. Boston Spa: Dept. Scient. & Indust. Res. National Lending Library for Science and Technology, Yorkshire. [40s. each part.]

[This review is also published in the *NLL Translations Bulletin of the Department of Scientific and Industrial Research*, April 1961. The original Russian book was published in Leningrad in 1959.]

The rapid increase in the incidence of carcinoma of the lung which has been occurring throughout the world during recent decades has stimulated research into the distribution and effects of carcinogenic substances in man's environment. Professor Shabad has played a leading part in the study of experimental carcinogenesis in the Soviet Union during the past 30 years and with his colleague, Dr. Dikun, he has in this monograph surveyed much of the historical background leading up to the current interest in carcinogens in the air. Although each of the 8 chapters is written around a particular aspect of the problem there is a great deal of overlap between them and in this translation the salient features of the book have been presented as Part A and the remainder is available as Part B.

Detailed results on the detection and estimation of carcinogenic material in soot and in atmospheric samples are given in Chapter 5 (Part A). The tables relate mainly to "snow" and other "sedimentation" samples but the limited number of results from "aspiration" samples show that atmospheric concentrations of 3:4-benzpyrene are in general much lower in towns in the Soviet Union than in comparable British towns. Reference is made to some exceptional figures obtained in the vicinity of an old coking plant, where concentrations of benzpyrene up to 0·4 mgm./m.^{3} had been recorded (at least 10,000 times the normal concentration in a British town). This plant has now been rebuilt, but it is interesting to note that the inhabitants of the village in which it was situated had been exposed to very high concentrations for many years, while the incidence of lung cancer there was not outstandingly different from that elsewhere. In this village samples were taken both by "sedimentation" and by "aspiration" methods, but the authors' comment that this provides a link between the results of the two methods in any locality is open to criticism. 3:4-benzpyrene has been detected in the lungs of town-dwellers by the Soviet workers, but the amounts have always been very small.

The remainder of Part A is devoted to the discussion and conclusions (Chapter 8) and this provides an adequate summary of the whole work for the general reader. The reasons for considering environmental factors in relation to lung cancer are stated at considerable length and the authors consider that exposure to specific occupational carcinogens and, more particularly, to 3:4-benzpyrene in urban atmospheres, has an important effect. The argument rests partly on the time-correlation, for in the Soviet Union the rapid industrialization and urban growth of recent decades has tended to increase the total amount of air pollution. Smoke from factories and houses is considered to be the main source of 3:4-benzpyrene, but the emissions from motor vehicles and the contribution from road dust are also mentioned. Attention is drawn to the feasibility of preventing smoke emissions in new installations, and the almost complete absence of 3:4-benzpyrene in the new Siberian town of Angarsk is of particular interest. The incidence of lung cancer there is being compared with that in the neighbouring old town of Irkutsk, but differences in age distribution and other factors will limit the value of this study. The authors have given serious consideration to the role of cigarette smoking, and a separate book is to be published on this subject, but they state here that 3:4-benzpyrene has been found in the smoke from Russian cigarettes in amounts similar to those found elsewhere.

Part B contains the remaining 6 chapters, each of which provides a detailed, but sometimes protracted, discussion of one of the above topics. The first deals mainly with the incidence of lung cancer within and

outside the Soviet Union. The evidence for a rise in incidence there comes mainly from necropsy data, and it is difficult to draw direct comparisons with other material, but it is stated that the current rates are significantly lower in the Soviet Union than in several other countries. There are differences between town and country and, as in Britain, the rate appears to decrease gradually from the largest cities to the smaller towns. Chapter 2 presents a historical account of the gradual recognition of occupational cancers, leading up to the production of cancer by pure hydrocarbons. It is based mainly on experience in other countries, but there is some reference to cases of tar cancer in the Soviet Union. The carcinogenic properties of hydrocarbons are considered further in Chapter 3 and emphasis is placed on 3:4-benzpyrene. The authors conclude that there is sufficient evidence to indict this compound as a cause of cancer in man and, in particular, as a cause of lung cancer. Chapter 4 is concerned solely with the methods of estimating 3:4-benzpyrene which have been used in the Soviet Union, and it contains a fundamental difficulty which mars the value of many of the observations. The merits of collecting samples by "aspiration" or by "sedimentation" are discussed and, contrary to the advice of some of their Soviet colleagues, the authors favour the latter. In many of their studies they have used a snow sampling method in which the deposit which has accumulated for some months on a mantle of snow is analysed. While this is extremely convenient it may bear little relationship to the amount of 3:4-benzpyrene suspended in the air, for most of it is contained in smoke particles which are too small to settle under gravity. Fluorescence spectroscopy has generally been used for the determination of 3:4-benzpyrene and a method of improving the precision by using solutions frozen in liquid nitrogen is described. Details are also given of a somewhat involved absorption method.

The various sources of 3:4-benzpyrene in a town are discussed in Chapter 6 and suggestions are made for preventing its emission. The problem is recognized as one concerning the incomplete combustion of fuel and emphasis is placed on industrial discharges, most of which are avoidable. Chapter 7 shows how improvements have been effected in some localities and gives details of the work undertaken in the new town of Angarsk. Here the residential area of the town is carefully isolated from all sources of pollution; most of the houses are served by a district heating system and a belt of woodland has been left between the industrial and residential parts of the town.

The book can be recommended to anyone who wishes to know more about work in the Soviet Union on this specialized subject of 3:4-benzpyrene in the air, but it is less useful as a general survey of the problem in urban atmospheres elsewhere. *R. E. Waller*

See also p. 316, STOCKS, **On the Relations between Atmospheric Pollution in Urban and Rural Localities and Mortality from Cancer, Bronchitis and Pneumonia, with particular reference to 3:4 Benzopyrene, Beryllium, Molybdenum, Vanadium and Arsenic.**

Occupational Hygiene

The order in this section is:—**General; Occupational Physiology; Occupational Diseases (Dust Diseases, Poisoning, Skin Diseases, Others); Occupational Psychology; Heating, Lighting and Ventilation.**

GENERAL

ANGLO-AMER. CORP. SOUTH AFRICA, LTD. **Medical Consultant's Report, 1959** [VAN BLOMMESTEIN, J. H. G.]. 60 pp., 1 fig. [1960.] Johannesburg: P.O. Box 4587.

The Anglo-American Corporation of South Africa is the largest mining organization in Africa. Its mining interests embrace gold mines in the Reef and in the Orange Free State, collieries in the Union of South Africa and in Southern Rhodesia, diamond mines in the Union and South-West Africa and copper mines in Northern Rhodesia. During 1959 the Corporation employed 146,581 African labourers in these undertakings. The labourers were recruited from various areas and tribes throughout Africa. No less than 35 ethnic groups were represented. This is an important matter as individual tribes have individual characteristics and habits, which require special consideration by managements responsible for their health, safety and welfare.

In this annual report, Dr. Van Blommestein, Medical Consultant to the group, gives details of the hospitals, clinics and medical arrangements generally provided for the care of the Africans. The whole constitutes an excellent comprehensive health and welfare service. Extensive information is presented in a series of tables covering statistics of mortality and morbidity from accidents and diseases and of lost shift rates.

In an admirable introduction great emphasis is placed on the preventive aspects of the medical and welfare work. It is interesting to note that Dr. Van Blommestein supports his theme by extensive quotations from the works of Charles Turner THACKRAH. An urgent and

vigorous plea is made for research into the most suitable diets necessary to maintain the African in full health and fitness for his arduous work. For too long, it is argued, the approach to this problem has been wrongly based on the African's dietetic habits rather than on the appropriate diet for the job.

[This report is confidently recommended for study by all doctors who are responsible for health, safety and welfare of Africans employed in mines, oilfields and large industrial undertakings.] *A. Meiklejohn*

BIRK, R. E. **A Clinical Survey of a Cross-Section of an Industrial Worker Group.** *Arch. Environment. Health.* Chicago. 1960, Oct., v. 1, No. 4, 291–6, 1 fig.

In recent years the medical profession has publicly advocated periodic health examinations as a means of early detection of disease and possible prevention of more serious disorders or complications. Many physicians, however, still question the value of such "well-patient" examinations in terms of diagnostic yield and ask whether the benefits warrant the expenditure in money and in examiners' time. In 1958 the author was presented with a unique opportunity to set up a prospective study of periodic health examinations on a relatively unselected, heterogeneous group of patients. "A welfare fund, having set aside funds for a health survey of employees under its jurisdiction, made available to these employees an opportunity for a medical evaluation." The 400 patients in this study, whose age, sex, race and employment status distribution are indicated in tabular form, "were thus unselected except in belonging to the much larger group under the jurisdiction of the fund and in their desire to have such an examination". [In the latter regard the subsequent findings would suggest that the group might, in fact, have been a highly selected one.]

All patients were examined by one of four internists and the initial examination included a complete history and physical examination, chest, photofluorogram, haemoglobin, white cell count, urinalysis, and serological tests for syphilis. Additional studies were carried out only if the initial findings indicated the need. A total of 1,279 diagnoses, or an average of 3·2 per patient, were reported to the patient or to his physician as requiring therapy or follow-up evaluation. Of note was the large number of conditions requiring therapy; 101 or 7·9% requiring surgical correction, and 844, or 66% requiring definitive medical therapy. Only 11·3% of the total "well-patient" study group were considered to be entirely normal. At the other extreme the diagnosis of proved or probable malignancy was made 19 times, and there were 21 patients with duodenal ulcer, 16 with arteriosclerotic heart disease with or without infarction, 8 with diabetes mellitus, and 2 in whom schizophrenia was diagnosed. Tables give the number of speciality department consultations and tests and their yield, indicating those persons requiring therapy, those requiring observation and those classified as normal.

1 to 2 hours was spent by the internist on the initial examination but by good organization the follow-up necessary to arrange subsequent clinical studies, correlate findings and prepare a report to the patient took up only 5 to 10 minutes of his time. The great majority of serious disease states had not been previously diagnosed or treated. The author concludes that this type of clinical survey, avoiding multiple screening procedures, has been justified by the results and could be extended with profit to larger groups. *P. J. R. Challen*

D'ONOFRIO, V. & MOSCI, L. La cataratta da calore indagine nei lavoratori siderurgici e nei vetrai. **[Cataract from Heat. Research on Metallurgic Workers and Glass Workers]** *Rass. Med. Indust.* Rome. 1960, July–Aug., v. 29, No. 4, 253–67, 6 figs. [26 refs.] English summary.

After an extensive review of the literature on "heat" or "glass-workers" cataract the authors, the senior of whom is the Director of the Institute of Industrial Medicine at Genoa, report on examinations carried out by them on operatives at A, a steelworks, and B, some small glass works.

A. They examined 597 steelworkers and found (1) cataract was just as frequent among those not exposed to thermo-luminous sources as in those who were; (2) the incidence of cataract among the workers did not differ from that found in the general population of the area; (3) there was nothing relevant regarding the length of time at work as similar lesions were found among those exposed for only a short time as in those with 15–20 years of service; (4) grave changes (senile cataract) were only found in older workers. There was only 1 case which might have been regarded as "heat" cataract. The authors therefore conclude that cataract in steelworkers is rare and arises only in association with certain physical and environmental conditions allied to constitutional and metabolic factors.

B. Investigations were then made in some small glass works employing in all 124 men, 74 of whom were over 40; 62 had more than 21 years at such work. There was direct exposure to strong thermo-luminous sources for an average of 4 hours per day, with vision naturally concentrated on such sources. The ambient temperature was high (in summer between 35 and 37°C.) and there was considerable contrast in luminosity between the ambient and the conditions at the work site. Although there had been recent technological improvements these had scarcely affected conditions for the master glass blowers at all. 5 men (all master glass blowers), the youngest of whom was 66, had cataracts of senile type, but no lens changes were seen among any of the workers which could be interpreted as occupational (posterior polar cataract).

If therefore it be accepted that it is the short infrared rays of 7,000–20,000 Angstrom units which in the past have been regarded as responsible for "glass-workers" cataract, the authors consider that present conditions both in the factories and as regard general living conditions are now such as to enable an individual to resist any possible harmful action of such rays.

[In none of the several interesting photographs was a glass worker using any form of eye protection.]

W. K. Dunscombe

LAWRENCE, Merle. **Some Physiological Correlates of Noise induced Hearing Loss.** *Indust. Med. & Surgery.* Miami, 1960, Oct., v. 29, No. 10, 445–52, 10 figs. [12 refs.]

Temporary threshold shift (TTS) audiometric measurements are often used to indicate the ability of a noise environment ultimately to produce permanent hearing loss in persons exposed to it. The TTS is never a pure measure of changes within the organ of Corti (the locus of damage due to noise), however, as changes along the nerve pathways also contribute.

The isolation of the responses of the organ of Corti from those of the nerve has been carried out in guineapigs by the use of electrodes, placed on the round window and in the temporalis muscle, to record cochlear potentials. Results from experiments carried out in this way are reviewed in this article.

As the sound stimulus applied to the ear is raised, the response increases to a maximum level, after which point further increases of stimulus cause a decrease in electrical response. At this point temporary damage is being produced in the organ of Corti. Further increase in stimulus produces further decrease in response and ultimately injury occurs.

Experiments on an ear previously overstimulated showed that increase of the stimulus up to 3 decibels above that required to give maximum response caused only small decreases in response—apparently due to severe overloading of a partially damaged system. Further increase in stimulus, however, caused a sudden break in response, after which maximum output was not again achieved. A similar break in response was noted after overstimulation at a steady level had been contiued for several minutes. Permanent loss of function has thus been demonstrated to occur rather suddenly both with increasing stimulus level and with tone duration. An organ of Corti suffering from previous overstimulation is more susceptible than a normal ear.

In a group of guineapigs subjected to overstimulation, electrical audiograms taken immediately after, and then after a period of 2 months showed that 60% showed various degrees of recovery, 10% maintained the same sensitivity, and 30% became less sensitive. Histological studies indicated that marked functional recovery of the organ of Corti may occur only when Reissner's membrane remains intact.

2 of the practical implications arising from this useful paper are that (a) not all individuals, if removed from a noisy environment will regain some of their lost sensitivity and (b) the exposure to noise of an individual suffering loss of hearing due to an inner ear involvement could be most unwise. *D. E. Hickish*

KYLIN, B. Undersökningar över hörseltrötthet och hörselskador efter exposition för monotont buller. **[Temporary Threshold Shift and Auditory Trauma following Exposure to Steady-State Noise]** *Nordisk Hyg. Tidskr.* 1960, v. 41, Nos. 11/12, 235–68, 9 figs. [Numerous refs.]

The English summary appended to the paper is as follows:—

"The main principle in the investigation has been to establish, through experimental studies of the temporary auditory threshold shift after exposure to noise, the relation between different octave bands of noise with respect to their 'potential damage risk', and to adapt the established relation, through field studies, to apply to long-term daily exposure to steady-state noise.

"The *experimental studies* were carried out on 220 normal-hearing young individuals, who were exposed to octave bands of noise during a two-hour period. Five different octave bands of noise, from 75–150 cps up to 4,800–10,000 cps, were used in the experiments. The octave-band pressure levels ranged from 75 to 115 dB. Ten test subjects were exposed to each octave-band pressure level. Each subject was exposed only once. An audiogram was recorded immediately before and another 15 minutes after the exposure.

"From the results it was possible to determine the relation between the different octave bands with respect to their capacity for causing temporary threshold shifts. It was shown that the 75–150 cps band needed about a 20 dB higher octave-band pressure level than the 2,400–4,800 cps and 4,800–10,000 cps bands to produce a significant threshold shift. The relation between the octave bands paralleled the equal-loudness curves as calculated by Beranek. In the highest octave band, 4,800–10,000 cps, however, there was a discrepancy, amounting to about a 10 dB lower octave level than that indicated by the equal-loudness curve.

"It has thus been possible to determine the relation between the sound pressure levels of the different octave bands with respect to a 'damage risk level' for exposure to steady-state noise.

"The *field studies* comprised auditory examinations and noise measurements carried out in a number of industrial plants. In about 15 different plants altogether 89 male workers were examined. The subjects were aged from 30 to 40 years and had worked in the same constant noise environment for the last 10 to 15 years before the time of this investigation. The noise investigated was of a single given frequency type, so-called flat noise. The over-all sound pressure levels ranged from 80 to 103 dB. The audiograms of the noise-exposed workers were recorded both before and after a working shift.

"The results show that exposure to the investigated noise at an over-all level between 80 and 84 dB did not generally cause any deterioration of the auditory status in relation to that of a control group. After exposure to noise with an over-all level of 85–89 dB, a statistically significant hearing loss had occurred at the 3,000, 4,000, 6,000 and 8,000 cps test frequencies, and exposure at the 95–99 and 100–104 dB levels has affected the auditory threshold at all frequencies tested. There was a marked 'dip' in the mean group audiogram in the frequency range between 2,000 and 8,000 cps.

"It was possible on the basis of the results, by a parallel shift of the 'equal-traumatic curve' obtained from the experimental studies, to determine a risk-level range for steady-state broad-band noise under which no or negligible mean hearing losses should occur after daily exposure over a long period. If noise at any octave level exceeds this range, relatively appreciable mean losses occur."

BANIK, E. Eine neue Maschine zum gefahrlosen Montieren und Abziehen von Autoreifen. **[A New Machine for Fitting and Removing Motor Tyres without Risk of Accident]** *Zent. f. Arbeitsmed. u. Arbeitsschutz.* 1960, Oct., v. 10, No. 10, 233–5, 5 figs.

Accidents during the fitting and removing of motor tyres by hand are becoming more frequent each year and occur particularly when the tyres are of large size. Experience has shown that most of these accidents are severe and lead to death or total or partial permanent disablement. The ways in which these accidents occur are shortly stated. There follows a technical description with 5 illustrations of machines (made by N. Th. J. Collmann and Co., Lübeck) operated by pneumatic power which will do the work of fitting and removing tyres safely and efficiently without any substantial physical exertion of the workers. In the bigger of the 2 machines there are 6 claws which work on the wheel rims to press off or draw on the tyres and there is a smaller somewhat simpler model with 2 claws which can also be used with all sizes of tyres. Additional advantages claimed for these machines are that with their use there is less wear and tear of materials and a great saving of time as a tyre can be changed in a very few minutes.

M. E. Delafield

See also p. 366, PUNTIGAM **[Tularaemia in Workers in Beet Sugar Factories]**.

OCCUPATIONAL PHYSIOLOGY

LIND, A. R. **Determination of Environmental Limits for Everyday Industrial Work.** *Indust. Med. & Surgery.* Miami. 1960, Nov., v. 29, No. 11, 515–18, 4 figs.

It has long been established that the body temperature increases during work, and several years ago NIELSEN showed that, over a wide range of environmental temperatures, the level to which the body temperature rose during work was dependent on the rate of work and independent of the environment. It is evident, however, that with a steady rate of work progressive increase in the temperature of the environment must eventually lead to a further increase in body temperature, probably as the result of readjustment of the thermoregulatory processes, and that this might well provide a physiological criterion by which to decide the limits of environmental conditions for everyday work.

The author describes some exploratory experiments carried out on a single subject. Each experiment lasted 1 hour. The subject was nude, except that he wore plimsolls while he walked on a treadmill. He walked continuously except for a pause of less than 40 seconds for weighing after 45 minutes. The energy cost was 210 kcal./m².hour. The effective temperatures in different experiments varied from 13° to 31·5°C. The rectal temperature reached equilibrium within the period of 1 hour, at approximately the same value (37·8°C.±0·1°C.) over the range of effective temperature from 13°C. to about 27° or 28°C. At higher effective temperatures the rectal temperature reached equilibrium at higher levels.

It is suggested that the reason for the rise of rectal temperature in the hotter climates is that the bodily thermal gradient has reached the minimal value compatible with the amount of metabolic heat that has to be transferred to the periphery without undue strain of the circulatory system. If the results described are supported by further experiments it seems that the limits of "neutral" zones for various rates of work might be used in defining acceptable climatic limits for industrial work.

Thomas Bedford

WYNDHAM, C. H. **Post-Absorptive and Resting Physiological Values of some Bantu Mine Recruits.** *South African J. Med. Sci.* 1960, Sept., v. 25, Nos. 2/3, 41–6.

Few acceptable measurements of the basal and resting metabolism, the heart rate and the body temperature of Bantu in South Africa have been published. The author reports measurements on 20 Bantu, from different tribal areas, under conditions which conformed rigidly with post-absorptive standards. In addition the resting metabolism, heart rate and rectal temperature were measured on two larger groups of Bantu selected at random.

On the first group of 20 subjects observations were made on first arrival at the mine, after 1 month of work, and again after 4 months of work. The results obtained are compared with the results of observations on European naval ratings in Singapore. The Bantu were significantly shorter and lighter than the naval ratings. They were considerably lighter than a group of Bantu (Shangaans) studied by POLITZER and ANDERSON (*South African J. Med. Sci.*, 1957, v. 22, 23). The oxygen consumptions of the 20 Bantu were significantly greater than those of the naval ratings.

In the Singapore observations quoted the average oxygen consumption measured on 4 successive days declined from day to day. In the Bantu there was a marked decline from the first to the second observation, and the fall in oxygen consumption accompanied a decline in the heart rate.

The author discusses the criteria necessary to establish that a subject is in a truly basal state, and suggests that

one possible method of determining the basal metabolism would be to measure post-absorptive oxygen intakes on 6 successive days, and to accept the measurements only if the values obtained on the last 3 occasions do not differ significantly from each other. *Thomas Bedford*

BROUHA, Lucien. **Physiology in Industry. Evaluation of Industrial Stresses by the Physiological Reactions of the Worker.**

This book is reviewed on p. 103.

OCCUPATIONAL DISEASES

HODKINSON, J. R., CRITCHLOW, A. & STANLEY, N. **Effect of Ambient Airspeed on Efficiency of Thermal Precipitator.** Reprinted from *J. Sci. Instruments.* 1960, May, v. 37, 182–3, 1 fig.

Tests of the sampling efficiency of standard and long-period thermal precipitators, by using coal dust particles and counting these in the 1–5 micron range of diameter, show that no significant change takes place when the wind speed past the instrument varies from 40 to 1,200 feet per minute. *C. N. Davies*

HODKINSON, J. R. **Reproducibility and Correlation of Long-Period and Short-Period Thermal Precipitator Samples of Airborne Dust in Mines.** *Ann. Occup. Hyg.* London. 1960, Nov., v. 2, No. 4, 235–42, 2 figs. [21 refs.]

The standard thermal precipitator is used for sampling dust over a short period, so that to ascertain the average dust concentration during a working shift, say in a mine, it is necessary to take a number of samples successively. There is now available a long-period thermal precipitator, which is compact and portable, and which samples continuously and unattended for 8 hours.

The author has studied the reproducibility of measurements of the mean concentration of airborne dust during a working shift in mines. In return airways of collieries the long-period instrument and 2 standard short-period thermal precipitators were set up. The long-period instrument sampled for 4 hours while 8 pairs of samples, each covering 25 minutes in every half hour were taken by the 2 short-period instruments. The results obtained were then subjected to regressional analysis.

It was concluded that the reproducibility of measurements with the long-period thermal precipitator at the 95% confidence level was approximately 20%. That is to say, if a single measurement of dust concentration is made there is a 95% likelihood that the mean of a very large number of such measurements made in the same dust cloud would lie between ±20% of the value obtained in the single measurement. For the concentration given by the 8 short-period samples the reproducibility was about ±35%.

In the absence of appreciable overlapping of dust particles on the glass slides there was no significant bias between the long- and short-period instruments. Where the overlap error in the short-period instrument is appreciable, the long-period instrument, with which there is little overlap in most mining conditions, gives a higher value. *Thomas Bedford*

HAMILTON, R. J. **Dimensions of Microscope Eyepiece Graticules.** [Correspondence.] *Brit. J. Applied Physics.* 1959, Sept., v. 10, No. 9, 428, 1 fig.

The graticule discussed (see HAMILTON *et al.*, *Brit. J. Applied Physics*, 1954, Supplement 3, p. S 101) was designed for the National Coal Board routine sampling programme, in which the size range counted is 1–5 microns for coal and 0·5–5 microns for rock. 2 sizes of graticule are made, 1 for Ramsden and 1 for Huygenian eyepieces, and the grid length is equivalent to 50 microns. The original grids were, however, too small so that larger ones are recommended. Tolerances are specified, and attention is drawn to the need for a standard of accuracy for eyepiece graticules: none now exists, and some graticules marketed show large discrepancies.
J. McK. Ellison

HOLT, P. F. & YOUNG, D. K. **A Dust-Feed Mechanism suitable for Fibrous Dust.** *Ann. Occup. Hyg.* London. 1960, Nov., v. 2, No. 4, 249–56, 8 figs. (1 on pl.).

Apparatus which is satisfactory for maintaining a dusty atmosphere for inhalation by experimental animals when ordinary dusts are used is unsatisfactory with fibrous dusts like asbestos. The fibres tend to form fluff balls, or to mat and cause jamming of the apparatus.

Breaking up the material in a high-speed disintegrator and removing the smaller particles, as formed, in a stream of air seemed to be a promising method, but it required a suitable disintegrator, capable of prolonged running without failure, which would not contaminate the material. The apparatus finally adopted is described in detail. It will maintain a dust-laden atmosphere at a reasonably steady level for long periods automatically. There is a simple method for varying the dust level, and there are adequate safeguards against failure.

Thermal precipitator samples show that an atmosphere containing 3,000 dust particles per cc. can be maintained. The particle size distribution in the experimental dust tunnel is very similar to the size distribution observed in the carding room of an asbestos factory.
Thomas Bedford

DAVIES, C. N. **Deposition of *Lycopodium* Spores upon Glass Slides exposed in a Wind Tunnel.** *Brit. J. Applied Physics.* 1960, Dec., v. 11, No. 12, 535–8, 4 figs.

The deposition of airborne dusts is of fundamental importance both in mines and in towns subject to air

pollution. In this valuable paper the author re-examines experimental data obtained by other workers (in particular those of GREGORY and STEDMAN, *Ann. Applied Biol.*, 1953, v. 40, 651).

He deals first with the results which Gregory and Stedman got when microscopic slides were placed horizontally in a wind tunnel, lying parallel to the air flow. He agrees with them that at very low speeds (less than 50 cm. per second) the deposition is by gravity, but points out that at intermediate speeds (50–320 cm. per second) the deposition they observed was due to (1) impaction on the "leading edge" of the slide, leaving a particle-free layer of air near the slide; and (2) gravitational fall of particles through this layer. At high speeds he attributes deposition to turbulence in the tunnel, which imparts to the particles enough energy to project them through the non-turbulent layer of air near the slide.

The results obtained by Gregory and Stedman for inclined plates are also discussed and related to the experiments of AMELIN and BELYAKOV on deposition on cylinders (*Dokl. Akad. Sci.* U.S.S.R., 1956, v. 108, 31) and to those of DAWES and SLACK in a duct in observations in a mine gallery [this *Bulletin*, 1955, v. 30, 521]. The author concludes that violent turbulence on a coarse scale relative to the stopping distance of the particles in still air caused deposition on all sides of an obstacle: milder turbulence caused deposition on the lee side only, where eddies induced by the obstacle play a part.

J. McK. Ellison

PFEIFFER, A. **A Simple Mathematical Method for Evaluation of Data from Droplet Counts on Settling and Inpaction Slides.** *Amer. Indust. Hyg. Ass. J.* 1960, Dec., v. 21, No. 6, 526–8, 2 figs.

MITCHELL, R. I. **Retention of Aerosol Particles in the Respiratory Tract. A Review.** *Amer. Rev. Respiratory Dis.* 1960, Nov., v. 82, No. 5, 627–39, 7 figs. [58 refs.]

A non-critical review of experimental results on the deposition of inhaled particles in the lungs. The mechanisms at work are not analysed, with the result that several important features are overlooked. These include the importance of particle shape in causing the interception of elongated particles, such as asbestos fibres; the considerable deposition of fine particles by Brownian motion in the upper respiratory tract and trachea; the difficulty of distinguishing between alveolar and bronchiolar deposition; the important distinction which has to be drawn between deposition and retention, the latter term being incorrectly used throughout the paper instead of the former.

An illustration of the lung bears a caption stating that particles larger than 2 microns fail to reach the alveoli, which is both incomplete, because it is not qualified by particle density and shape, and incorrect except in rather extraordinary circumstances.

Quotations and illustrations from the original papers are freely used but there is no discussion of the reliability of the results. *C. N. Davies*

MINISTRY OF LABOUR. **Dust in Card Rooms. Fourth Interim Report of the Joint Advisory Committee of the Cotton Industry** [BETTENSON, A. S., Chairman]. 18 pp., 8 pls. & 1 chart. 1960. London: H. M. Stationery Office. [2s.]

This Report describes a new device (Selrow) for controlling dust emitted from carding engines. It consists of sets of tubes, connected to exhaust ducting, which are inside enclosures containing the dust liberated at the three dustiest points on the carding engine. In normal working conditions, the device is said to have an overall efficiency of about 62% for removing dust particles ranging from 0·5 to 10 microns. *R. S. F. Schilling*

KLEINFELD, M. & MESSITE, Jacqueline. **Problem Areas in Pneumoconiosis.** *Arch. Environment. Health.* Chicago. 1960, Nov., v. 1, No. 5, 428–37, 11 figs.

The problem areas in pneumoconiosis are grouped under 3 main headings: (1) the establishment of causal relationship; (2) the evaluation of the degree of disability; and (3) the medico-legal factors. Among particular matters discussed are the importance of detailed ascertainment of the employment history, the environmental factors and the quality, quantity and particle size of the dust. Various methods of measuring pulmonary function are reviewed and their limitations noted. Finally, reference is made to the varying pattern of legislation for compensation of pneumoconiosis in the various states in U.S.A. *A. Meiklejohn*

BALGAIRIES, E. & PRÉVOST, D. Pneumoconio-tuberculose et gastrectomie. [**Gastrectomy in Pneumoconiosis with Tuberculosis**] *Arch. Malad. Professionnelles.* Paris. 1960, Sept., v. 21, No. 9, 561–4, 2 charts.

The question of a relation between gastrectomy and the appearance of tuberculosis in the general population was discussed by DUPUY and MAILHO in 1959 at a meeting of the French Society of Gastro-Enterology. They observed 500 gastrectomy cases over a period of 9 years and found active tuberculosis in 46, a percentage of 9·2. The only paper known to the authors on the supervention of tuberculosis in pneumoconiotic subjects who had been subjected to gastrectomy was by VOGLIAZZO. He did not find that gastrectomy favoured the development of tuberculosis in the course of 3 or 4 years.

The present study compares the effect of gastrectomy on 206 colliers with pneumoconiosis with that on 249 non-pneumoconiotic coal-miners, over a period of more than 15 years. The pneumoconiotic group yielded 26 cases (12·62%), the non-pneumoconiotic 5 (2·004%).

Figures are then given of the percentage of tuberculosis cases found in ordinary coal-miners (0·23%) and in pneumoconiotic coal-miners (4·29%). Gastrectomy lead to an increase of three times the number of tuberculosis cases in pneumoconiotics, and of 60 times the number in non-pneumoconiotic miners. These figures however, when submitted to a statistician did not find approval, although it was agreed that gastrectomy probably favours the appearance of tuberculosis in pneumoconiosis cases.

The authors show graphically that in the 26 cases the

tuberculosis appears in the first 10 years after the operation, in the older cases, however, it appeared later. Where radiological films had been taken before the operation lesions of a tuberculous nature were observed. The pneumoconiosis itself is not influenced by gastrectomy.

The points raised in this paper, say the authors, should be discussed when surgical intervention is suggested for a pneumoconiotic case. From the occupational medicine standpoint, the supervision of the pneumoconiosis case with a gastrectomy should be particularly careful.

Charles L. Sutherland

GERNEZ-RIEUX, C., BALGAIRIES, E. VOISIN, C. & FOURNIER, P. **Pneumoconio-Tuberculosis. Results of Medical and Combined Medical-Surgical Therapy.** *Amer. Rev. Respiratory Dis.* 1960, Dec., v. 82, No. 6, 835–42, 3 figs. [23 refs.]

In France in 1957 the incidence of pulmonary tuberculosis in 25,547 pneumoconiotic miners was 4·29%. Treatment is therefore important. 395 patients with pneumoconiosis and tuberculosis were investigated in hospital in Lille between January, 1952, and March, 1958. Diagnosis was made by the occupational history, radiographic or pathological examinations or both, and by sputum examinations for tubercle bacilli.

The medical treatment given for 6 months was streptomycin daily, PAS and isoniazid. A double drug regimen was used for long-term therapy (isoniazid with PAS, cycloserine, viomycin or ethionamide). In a few cases steroid therapy was used but this was inefficient and dangerous.

The therapeutic efficacy of the medical and medical-surgical therapy was based on the criteria of closure or eradication of cavities proved by radiographic examinations, and reversal of infectiousness. Reversal of infectiousness was considered to have occurred when smear, culture and inoculation tests were negative for 6 months. A distinction has been made between healing (closure of cavity and reversal of infectiousness), and improvement (reversal of infectiousness only). The results were that in 277 cases there were 69 cases of cavity closure and non-infectious sputum.

The percentage of good results was higher in pneumoconiosis with discrete opacities than in pneumoconiosis with massive shadows, and in limited tuberculous lesions it was high compared with those in advanced cases. A comparison was then made of results of chemotherapy in a group of miners with discrete opacities, a group of miners with at least 10 years' exposure but no pneumoconiosis on radiographic examination, and a group of non-miners. The percentage of healing for comparable tuberculous lesions was only half as great in coal-miners as in patients who had never worked in a coal-mine.

The relative failure of chemotherapy justifies surgical intervention. 118 patients had surgery (lobectomy is the best operation) after chemotherapy (except in 2). Of the 116 patients followed from 2 to 7 years, 81 were healed and 39 went back to work. The results justify surgical therapy after pre-operative chemotherapy for 6 months without radiographic improvement and when functional respiratory values and extent of the tuberculous lesions make it possible. *Charles L. Sutherland*

CHARBONNIER, J. & COLLET, A. À propos de la théorie de la solubilité dans la pathogénie de la silicose. **[The Solubility Theory of the Pathogenesis of Silicosis]** *Arch. Malad. Professionnelles.* Paris. 1960, Sept., v. 21, No. 9, 534–43. [97 refs.]

The solubility theory, as commonly understood, explains the effect of silica as caused by a product dissolved from the silica and acting at a distance from the particles. This does not now fit in with known experimental facts. It was considered worth while at a time when the theory seems about to be abandoned, to review the problem critically. The review comprises a study of experimental work carried out from 1922, GYE and PURDY (*Brit. J. Exper. Path.*, 1922, v. 3, 75) to 1960, CHARBONNIER *et al.* [this *Bulletin*, 1960, v. 35, 860] and includes information derived from GARDNER, KING, POLICARD and others.

The facts are that the product of the solution of silica is not toxic, and it is not related quantitatively in any constant way to the toxic or fibrogenic effects of the particles. Silica particles cannot transmit their toxic properties to any distance although colloidal silica may do so. The conclusion is that phagocytosis is necessary; so that there is a close contact between the surface of the particle and the cytoplasm. The crystalline structure of silica only determines the intensity of the reaction, not its nature, because amorphous silica is not devoid of toxicity. From their own experience the authors have found that the phosphates of aluminium are non-toxic so that the crystalline structure alone is not sufficient to produce toxicity. An insoluble crystalline silica is inert so that a degree of hydration is necessary to make a silica particle toxic.

From this it is concluded that the toxic effects of the silica particle come from a superficial layer of hydrated silica. Admittedly this is a working hypothesis and that certain points have still to be cleared up such as the question of the effect of the crystalline structure on the intensity of the condition and the influence of etching produced by hydrofluoric acid and by caustic soda.

Charles L. Sutherland

CLAEYS, C. & QUINOT, E. Notions nouvelles sur la pathogénie immunitaire de la silicose. **[New Ideas on the Immunological Pathogenesis of Silicosis]** *Arch. Malad. Professionnelles.* Paris. 1960, Sept., v. 21, No. 9, 553–7. [35 refs.]

The association of silicosis and rheumatoid arthritis in the Caplan-Colinet syndrome suggests that these diseases may have a common factor in their pathogenesis, and rheumatoid arthritis has undoubtedly an immunological basis. So far as silicosis is concerned, however, only the laboratory provides any evidence. ISHINISHI and MIYAZACKI, (*C.R. Journ. Françaises Path. Minières*, Paris, 1958, 319) in Japan and ANTWEILER and HIRSCH in Germany [this *Bulletin*, 1956, v. 31, 1111, 1232] showed that rabbits subjected to repeated injections of silica formed an agglutinating antibody against a silica-protein complex in the serum. Later other Japanese authors have shown the existence of a similar action apparently less specific, in the human serum. Some support is given

to the hypothesis by silicotic lesion itself; the ring of cells formed round the silica particles is composed of plasmocytes, which secrete globulins. PERNIS *et al.* have shown by electrophoretic separation that the silicotic nodule is a depot of serum gamma globulin, that is, of antibodies. From these facts VIGLIANI put forward the immunity hypothesis [see VIGLIANI and PERNIS, this *Bulletin*, 1961, v. 36, 1].

Quartz itself is unlikely to act as an antigen; the acting antigen is probably composed partly of silica and partly of a substance drawn from the living material itself. The antibodies demonstrated by Ishinishi and Antweiler have always acted on a complex of protein and quartz.

It is probable that there is adsorption of protein compounds on the surface of the crystal itself. Ishinishi and Miyazaki have shown that the antibodies in the rabbit are specific for the crystalline form of the silica, but this has not been confirmed by Antweiler and Hirsch.

These antibodies in the serum may not be the antibodies concerned in the production of the silicotic nodule. The antibody responsible is to be considered as coming originally from cells which have phagocytosed the silica, and not from the serum. One cannot conceive a localized disease if the antigen, or a part of it, is not fixed. Silicosis is not a generalized disease.

The close relation between silicosis and tuberculosis, according to the authors, does not present any support to an immunological action of silica.

Charles L. Sutherland

ROWSELL, E. V., NAGELSCHMIDT, G. & CURRAN, R. C. **The Effects of Dusts on Peritoneal Cells within Diffusion Chambers.** *J. Path. & Bact.* 1960, Oct., v. 80, No. 2, 337–44, 14 figs. (13 on 4 pls.) [16 refs.]

The unique effect of silica *in vivo* is the proliferation of fibroblasts and the deposition of massive redundant amounts of collagen round the dust. Injury to phagocytic cells may be the stimulus to fibrous tissue formation. The diffusion chamber technique is here used in an attempt to show if macrophages and silica together could liberate a diffusible toxin which could cause fibrosis in the tissue outside the chamber, and also if silica stimulates the macrophages to fibroblastic activity as it does when free in the tissues.

The method of construction and use of chambers is described and the experiment consisted of inserting chambers into the peritoneal cavities of rats. The chambers contained cells alone, cells and tridymite, cells and felspar, cells and diamond dust. Empty cells were also used to check the possibility of leakage. Each rat received 2 chambers.

Most of the cells in the chambers soon died, whether dust was present or not. Often, however, they did not autolyse, and their corpses could be seen months later. In a few days fibroblasts began to grow; their growth was dense in the dust-containing chambers. Silica however was no more effective in this way than the other dusts.

The chambers containing fibroblasts and silica did not show any release of toxin: in fact no substance irritant to the tissues was liberated from any chamber. Silica had no effect on the viability of the fibroblasts within the chambers. All dusts however affected the behaviour of the fibroblasts in the same fashion.

The question is discussed whether the fibrogenic activity of silica dust is potentiated when inert dusts are present to stimulate the fibroblasts.

Charles L. Sutherland

VIGLIANI, E. C., PERNIS, B. & BOLIS, L. **The Acute Toxic Effect of Intravenously Injected Tridimite Dust.** *Med. d. Lavoro.* 1960, Oct., v. 51, No. 10, 575–8, 1 fig.

Colloidal silica injected intravenously in animals produces sudden death by anaphylactic "silica shock". Excessive doses of crystalline silica also produce this but MARKS *et al.* [this *Bulletin*, 1959, v. 34, 348] have shown that death may be delayed for 7 to 14 days by using more moderate amounts of tridymite dust. The authors repeated this experiment and studied the lesions produced in the liver and spleen. These lesions were similar to those produced by endotoxins adsorbed from the intestinal tract.

To test this, mice were treated with chloramphenicol or tetracycline for 14 days before injection of tridymite, to reduce the intestinal flora. The number of deaths at the end of 10 days in the mice treated with antibiotics and tridymite averaged 20% as compared with 70% in mice treated with tridymite alone.

Cortisone protects from the lethal effect of endotoxins. Mice were treated with cortisone for 3 days before intravenous injection of tridymite. It provided complete protection.

These experiments support the possibility that delayed shock which follows the injection of tridymite may be due to the action of endotoxins adsorbed from the intestinal tract. Tridymite dust is capable of inducing the degeneration of macrophages *in vivo* and the authors link this action with the processes leading to the delayed effect of the dust.

This delayed effect may be due to lack of detoxication of the endotoxins in the reticulo endothelial system or to increased susceptibility to endotoxins in mice treated with tridymite dust. RILKE & PERNIS (Communication to Int. Conference of Histochemistry, Paris, Sept. 1960) showed that mice were more susceptible to the lethal effect of endotoxins when injected previously with tridymite. *Charles L. Sutherland*

SAFFIOTTI, U. **The Histogenesis of Experimental Silicosis. I. Methods for the Histological Evaluation of Experimentally Induced Dust Lesions.** *Med. d. Lavoro.* 1960, Jan., v. 51, No. 1, 10–17. [Numerous refs.]

This is the first of a series of papers which are to be published on the histogenesis of experimental silicosis. It is entirely concerned with a detailed exposition of the methodology and the arbitrary special classification of the various grades and phases in the development of silicotic fibrosis which are to be followed. Previous classifications of the lesions induced by fibrogenic dusts are considered to be inadequate for recording the histogenesis of silicotic lesions. Moreover, a re-examination

of the morphology of experimental silicosis was deemed necessary in view of the recent immunological approach to its pathogenesis. *A. Meiklejohn*

EBINA, T., TAKAHASHI, Y. & HASUIKE, T. **Effect of Quartz Powder on Tubercle Bacilli and Phagocytes.** *Amer. Rev. Respiratory Dis.* 1960, Oct., v. 82, No. 4, 516–27, 11 figs. [16 refs.]

Tuberculosis is regarded as the most common complication of silicosis and the prognosis of the combined disease is serious. At the Research Institute for Tuberculosis and Leprosy, Toboku University, Sendai, Japan, a programme of experimental studies was undertaken to study the effect of quartz powder on tubercle bacilli and phagocytosis. 5 experiments, 2 *in vivo* and 3 *in vitro*, were completed; details of the methods of each experiment are fully set out.

It was observed in mice that quartz particles injected subcutaneously stimulated the growth locally of BCG which had been subsequently inoculated intravenously. By contrast where non-siliceous particles, such as bismuth subnitrate, were used practically no multiplication of BCG was observed. The intravenous administration of quartz particles increased the susceptibility of mice to BCG when injected by the intravenous route.

In the experiments *in vitro*, no multiplication of BCG was observed in the mononuclear phagocytes which had ingested non-siliceous dust particles. Siliceous particles, including quartz, sericite and kaolin, caused considerable destruction of mononuclear phagocytes.

The authors submit that the results of their experiments suggest that the great destruction of mononuclear phagocytes may be one of the causative factors which considerably enhance the multiplication of tubercle bacilli in silicotic foci. *A. Meiklejohn*

SHELLEY, W. B. & HURLEY, H. J. **The Pathogenesis of Silica Granulomas in Man: a Non-Allergic Colloidal Phenomenon.** *J. Investigative Dermat.* 1960, Feb., v. 34, No. 2, 107-22, 13 figs. [27 refs.] Discussion 122–3.

This paper opens with a discussion on silica granuloma of the skin and of the various forms of free silica and silicates. The authors investigated the pathogenesis of the condition and directed their study towards exploring the possibility that the reaction is due to local colloid production.

Groups of 10 healthy white and negro volunteers were used, and each group received intradermal injections of commercial fine sand, silicic acid, silica gel powder, asbestos (magnesium silicate), sodium silicate, and colloidal silica. The 4 first-named materials were in 1% suspension in saline, the sodium silicate in 1% solution (this was partly colloidal) and 2 slightly different solutions of colloidal silica were used in 0·01, 0·1 and 1% concentrations.

In no instance did the sand, silicic acid or silica gel produce a palpable response in the skin at 1, 2 or 4 weeks, and biopsy studies revealed no appreciable epithelioid response. 6 of the 10 men injected with asbestos showed a varying papular response which lasted well beyond one month and then slowly disappeared completely. Histological examination revealed asbestos threads, giant cells and epithelioid cells. Microincineration and treatment with hydrochloric acid revealed a surprisingly large amount of silicate material unsuspected in H and E preparations viewed with transmitted light. The 10 men who received sodium silicate solution all showed an inflammatory reaction. Ulceration was followed by papule formation persisting for over a month, and biopsy revealed a patchy granulomatous response. With colloidal silica none of the subjects showed a gross response to 0·01% dilutions; 6 of the 10 men showed a small papular response to 0·1% dilutions, the papule persisting for about 6 weeks; all showed a definite palpable response to 1% dilutions. 10 other men were injected with 1% dilutions and all 20 were repeatedly checked over a period of 8 months, during the latter part of which most of the lesions disappeared, leaving only 2 that were still evident at the end of the period. The serial biopsy studies showed that even at 24 hours occasional epithelioid cells were seen in the mixed inflammatory response, by 3 days a mixed round cell and phagocytic response was seen, and at 10 days this had differentiated into an epithelioid sarcoid type of reaction, fully developed at 2 months. The appearances are illustrated by excellent photo-micrographs. In these lesions the presence of silica was not evident from the presence of giant cells or of doubly refractile bodies. The only evidence of colloidal silica, other than the pure epithelioid response, was the persistence of a mineral ash despite microincineration at 600°C. for 90 minutes and treatment with concentrated hydrochloric acid for 30 minutes.

The authors conclude that the production of silica granulomas is a phenomenon dependent on the colloidal state of silica. Colloidal silica gels in the tissue, so that much of it is held there. The silica granulomas which arise clinically from large particles are the result of "weathering" in the body over a long period of years by a series of processes, hydration, ion exchange, oxidation and release of colloidal silica, which is the same as natural weathering but which proceeds more rapidly. Once a critical rate of release of colloidal silica is reached, granuloma formation begins, continuing for months or years until all the silica is ingested, when spontaneous resolution may begin. The possible formation of colloidal granulomas by other metals is referred to. The authors find no evidence that silica granulomas develop as a result of an allergic process, nor of piezoelectric effect. [Their remarks seem to be directed entirely towards natural and experimental silica granulomas of the skin but it seems to the abstracter that they are capable of being applied to these reactions in other organs.] *A. T. Doig*

MULLER, M., MARCHAND-ALPHANT, AMOUDRU & ORCIVAL. Silicose des ganglions mésentériques. [**Silicosis of the Mesenteric Glands**] *Arch. Belges Méd. Sociale, Hyg., Méd. du Travail et Méd. Légale.* 1960, July, v. 18, No. 7, 543–7, 1 fig. [10 refs.].

Extrapulmonary deposits of silicotic tissue are not unknown. They may be found in the skin, in the liver,

spleen and bones. In the kidneys particles of silica can be found in the endothelial cells of the capillaries. In advanced silicosis, glandular involvement is extremely frequent, and often there is a peripheral calcification producing the egg-shell appearance. Mediastinal glands are frequently affected but mesenteric glands more rarely.

The subject under consideration was a silicotic miner who died after a cerebral haemorrhage. The autopsy confirmed the presence of silicosis with nodulation and some masses showing ischaemic cavitation. There was a whitish glandular mass in the axillary region. The tissue was too necrotic to allow of detailed examination but the necrotic cells may have been neoplastic or histiocytic. The diagnosis of neoplasm was ruled out; histiocytic reaction is characteristic of glandular tissue to silica.

In the abdomen, at the bifurcation of the renal arteries there was a group of hard, black glands, one of which showed egg-shell calcification. One of the glands was the seat of necrosis similar to that of the axillary glands. The other glands were transformed into little silicotic masses. On microscopic examination the fibres were whorled, and stained with Van Giesen in the same way as silicotic fibres. Dust was present between the fibres.

By microincineration and treatment with hydrochloric acid, birefringent particles of silica were demonstrated. The particles of silica probably reached this position across the diaphragm, but they may also have been ingested.

It is exceptional for mesenteric glands to be affected to such an extent as in the present case. Abdominal silicosis is rare.

The authors suggest that the condition of the axillary glands was a distant reaction to the mesenteric silicosis.

Charles L. Sutherland

Le-Hir, M., Guerrero, A. J., Variot, J. & Bellanger, J. Quelques aspects de l'atypie de la silicose [**Some atypical Forms of Silicosis**] *Arch. Malad. Professionnelles.* Paris. 1960, Sept., v. 21, No. 9, 544–52, 3 figs. [11 refs.]

Radiology has been given priority in the diagnosis of silicosis; the earliest sign accepted is represented by the appearance of minute opacities in the lung parenchyma. Where radiological examinations are made regularly year by year, radiological changes may be found which cannot be placed within the usual categories of the Cardiff-Douai classification; these changes in their progression show themselves to be pneumoconiosis. Two atypical forms are considered:—(1) silicosis initially atypical; (2) atypical progression in established silicosis.

The first type is illustrated by a miner exposed to silica, who at first showed a small lesion at the right apex, but no change in the other parts of the lungs. In 4 years this lesion had greatly extended and a diffuse general nodulation had appeared. Later the lesion showed a cavity: and the sputum showed tubercle bacilli. Although the diagnosis of atypical silicosis is made, we are not informed if vigorous antibiotic treatment was carried out. Lung biopsy is suggested as a possible help in early diagnosis but it is preferable to await the progression of the condition.

The second type is illustrated first by a silicotic subject (category 3 p) who had an acute illness which cleared with antibiotic treatment. A year afterwards, however, bilateral massive fibrosis was present.

Another case was a miner who was in hospital after an acute illness accompanied by the production of black sputum. The radiological findings were a mass on the left side, and diffuse nodulation elsewhere. For various reasons a positive test for tubercle bacilli by gastric lavage was discounted. The man had been passed as clear earlier in the same year by miniature radiograph. Here again biopsy or even exploratory thoractomy may be advised especially as the possibility of cancer may arise.

Generally, however, the cases showing atypical progression, later on advance in the ordinary way. The progression of a pneumoconiosis is not uniform in workers exposed to the same risk; infection and constitutional factors modify the clinical aspect and produce temporary atypical variations. *Charles L. Sutherland*

Dalloz, C., Perrin, L. F. & Brune. Étude des résultats d'une épreuve d'effort standard chez les silicotiques en fonction des différents examens cliniques et biologiques et de l'enquête professionnelle. [**Results of a Standard Effort Test in Persons with Silicosis in Terms of Different Clinical and Biological Examinations and of the Occupational Investigation**] *Arch. Malad. Professionnelles.* Paris. 1960, Sept., v. 21, No. 9, 524–30, 2 figs.

The object of this study is to compare the results of physiological tests with, on the one hand the clinical and radiological examination, and on the other hand, with the results of enquiries from foremen and others as to the arduous nature of the work and the workman's ability to perform it.

71 miners and 31 potters, suffering from silicosis, were studied in 3 ways.

(1) Industrial history and clinical and radiological examination. The category of the pneumoconiosis was recorded according to the Cardiff–Douai classification. The most important part of the radiology was by measuring on the screen the movements of the diaphragm during inspiration and forced expiration and by observing the changes in transparency of the parenchyma of the lung during that cycle.

(2) Various physiological tests, the most important being the determination of the dyspnoea index of Wright.

(3) Enquiries from foremen and others regarding the type of work, the distance from the bottom of the pit to the working place and the foreman's opinion as to the workmen's ability to do the work.

The results were given graphically for miners and potters separately by plotting the dyspnoea index against the results of physiological tests, the results of screening, the work required by the employment and the radiological category. When the results of physiological tests were bad the dyspnoea index was high. The screening tests showed the same result. All workers on heavier work have a low dyspnoea index. The radiological categories of the miners had no relation to the dyspnoea index except in one early category case who gave a high reading. This may have been due to a concurrent

bronchitis. The graph for the potters suggests very strongly that the type of silicosis in potters is more serious than that in miners. The dyspnoea index of potters showing categories B, C and D is higher than that of miners of the same category and the same tendency is shown in categories 2 and A. *Charles L. Sutherland*

JAMES, Dinah M., MORRIS, T. G. & MARKS, J. **Drug Treatment of Experimental Silicosis.** *Brit. J. Indust. Med.* 1960, Jan., v. 17, No. 1, 36–40.

This communication deals with the treatment of mice which had received intravenous injections of silica, with a variety of drugs selected chiefly on the basis of their ability to protect phagocytes *in vitro*. The drugs were administered for periods of 6 to 12 weeks and at the end of that time the livers of the surviving mice and also some of those which died were examined histologically.

Compound 46–107 [this *Bulletin*, 1959, v. 34, 904] an organic base chemically related to compound 48–80 previously tested and found to inhibit the development of silicosis [MARKS, *et al.*, *ibid.*, 1959, v. 34, 348] lacks the latter's disruptive effect on mast cells. It was thus disappointing to find that although this drug afforded a considerable degree of protection, it had to be pushed to the point of toxicity to achieve this.

Aluminium has been used in relatively insoluble forms in previous experimental work and clinical practice. Soluble preparations, aluminium chelates with oxytetracycline, sequestric acid, and dextran were used in this study. The results were not very convincing; only the compound with normal dextran (a dextran of low molecular weight was also used) being effective, but all evincing toxic effects.

Of two phenazine compounds chosen as being the most active in *in vitro* tests, only one, B749, gave a degree of protection. Methylene blue also proved to be inhibitory. Single experiments not described in detail were made with certain other drugs.

It is pointed out that in evaluating the effect of these drugs, a high dose of a very fibrogenic dust, 3·5 or 5 mgm. of tridymite per mouse weighing about 20 gm., was administered. None of the drugs gave complete protection and all were toxic, but it is suggested that had less silica been administered more tolerable drug régimes could have been used with benefit. The authors claim for this study no more than that it indicates lines of research of potential value in eventually achieving a successful drug treatment of human silicosis.

A. T. Doig

MORROW, C. S. **The Results of Chemotherapy in Silicotuberculosis.** *Amer. Rev. Respiratory Dis.* 1960, Dec., v. 82, No. 6, 831–4.

This is a study of 18 miners who were treated for silico-tuberculosis in hospital at Wilkes-Barre, Pennsylvania, between 1 July, 1958, and 1 January, 1960. The diagnosis was made on the occupational history, the radiographic findings and examination of the sputum, smear and culture. All the miners had worked in hard-coal mines for 7 to 50 years. The therapy, which was given daily, was (1) in 10 patients, streptomycin, PAS, isoniazid and pyridoxine, (2) in 8 patients, isoniazid, PAS and pyridoxine, (3) in 2 patients whose sputum was still positive after 6 months therapy with (1) above, cycloserine and pyrazinamide were added and treatment was continued for at least 6 months.

The progress of the patients was checked by radiographic examination every 2 months, and monthly sputum tests. Reversal of infectiousness was regarded as having occurred if sputum smears and cultures were negative for at least 2 successive months.

The results were that in 11 cases radiographic improvement was shown by regression of non-cavitating disease. Reversal of infectiousness occurred in 16, but in no patient with cavities was there cavity closure. There were 3 deaths; one patient who remained positive died of myocardial infarction, the other 2 had reversal of infectiousness but died of non-tuberculous pneumonia superimposed on chronic bronchitis and emphysema. It was found that treatment by isoniazid-PAS regimen was as successful as the isoniazid-streptomycin-PAS regimen.

A previous report from the same hospital in 1958 [this *Bulletin*, 1959, v. 34, 135] on other patients was not so satisfactory. This was due to the fact that streptomycin was administered twice weekly instead of daily, moreover the patients were in an older age-group.

The conclusions reached from this study are that chemotherapy influences silico-tuberculosis favourably, particularly from the standpoint of sputum conversion. Further, isoniazid is an essential component of any drug regimen for effective therapy of the disease.

Charles L. Sutherland

ENGELBRECHT, F. M., THIART, B. F. & CLAASSENS, A. **Fibrosis and Collagen in Rats' Lungs produced by Radioactive Mine Dust.** *Ann. Occup. Hyg.* London. 1960, Nov., v. 2, No. 4, 257–66, 6 figs. (5 on pl.) [21 refs.]

The gold-bearing quartz conglomerate of the Witwatersrand, South Africa, is one of the most notoriously dangerous rocks with respect to its silicotic effect [this *Bulletin*, 1933, v. 8, 727]. The quartz rock contains radioactive material and the authors have examined whether it might be a contributory factor in producing silicosis.

Rats were used in the experimental work; they were injected intratracheally with mine dust samples (50 mgm. in each rat) of which the silica content ranged from 66 to 86% and differing radioactivity. Five different samples were used; those with a high radioactivity and low silica content produced significantly more collagen than those with high silica and low or no radioactivity.

No correlation was found between the amount of silica retained and the amounts of collagen produced in the lungs.

The whole series of observations was carefully prepared and continued for a period of 370 days. The authors are well aware of the difficulties that beset those seeking the essential causes of silicosis; they conclude that the presence of radioactive material might enhance the fibrogenic action of silica in the lungs of rats. They

point out the wide variation in man's susceptibility to silicosis:—"Some individuals after 10–15 years underground are not suffering from dust disease, while others are totally disabled within two years." *S. Russ*

EDENFIELD, R. W. **A Clinical and Roentgenological Study of Kaolin Workers.** *Arch. Environment. Health.* Chicago. 1960, Nov., v. 1, No. 5, 392–403, 8 figs. [24 refs.]

Extensive deposits of kaolin occur in the State of Georgia, U.S.A. Over 2 million tons were mined in 1957 and the demand is increasing because of the importance of kaolin in a wide range of industries, particularly the manufacture of paper, paints and pottery. The clay is removed from the mines in large moist lumps and at this stage presents no dust problem. But processing and refining for industrial uses frequently involves drying of the clay and as a result many workmen are exposed to high concentrations of fine dry dust. The physical and chemical characteristics of the dust are described. The SiO_2 in kaolin is combined with Al_2O_3; none of it is present in the form of free silica and it does not react physically or chemically as silica.

Among 1,130 workmen investigated 44 (3·7%) showed some radiographical evidence of pneumoconiosis. Of those, 31 were classified as discrete nodular pneumoconiosis and 13 as confluent pneumoconiosis. The author is of opinion that the lung changes observed in these kaolin workers do not represent silicosis. The discrete nodular cases appear to be due to retention in the lungs of fine kaolin dust which is almost completely inert in experimental animals, and in man does not cause any impairment of physical capacity for work. The cases of massive fibrosis are regarded as being due to the combination of tuberculosis and heavy dust exposure, which according to the terminology of GROSS is named tuberculopneumoconiosis [see this *Bulletin*, 1959, v. 34, 781]. *A. Meiklejohn*

CANTELLANO ALVARADO, L., ENRIQUEZ, J. de la L. & BARRON, D. Asbestosis. Estudio epidemiológico en una fábrica de articulos de asbesto cemento. **[Epidemiological Study in an Asbestos Cement Factory]** *Salud Pública México.* 1960, July-Sept., v. 2, No. 3, 557–66, 2 figs.

The authors visited this factory to enquire into the risk of health associated with the processes used, remarking that it was situated in a zone originally reserved for industry and since surrounded by dwellings in which, from contiguity, the hazards of the industry were inflicted on the inhabitants. Not only was a cement works nearby but also other factories emitting harmful dusts. In the works studied the raw materials were asbestos, Portland cement and a siliceous sand and plaster of Paris.

It was found that the method of reducing the sand to a suitably small size, by means of crushers and sieves, involved the escape of much dust into the air. The asbestos arrives in jute bags whence it is taken to be torn into small fragments in closed containers and removed from these by suction for storage in silos. To manufacture tubes, sheets and other products the asbestos is discharged on to a balance controlled by hand and later two persons lift it in a container for transport to another chamber into which cement and water are discharged until a paste of suitable consistence is formed. To give body to this a quantity of siliceous sand is added and the product is then shaped while being exposed to heat for 24 hours. For special purposes moulds of various forms are used, sometimes made of wax.

Remarking that asbestos disease of the lungs is notable for the early and severe pleural involvement, the authors point out that, at all stages of manufacture, precautions against dust injury are inadequate. In many stages these harmful materials are discharged onto open floors or platforms. The upkeep of the mill was so faulty that dust escaped from many points and a cyclone, used for extraction at one stage, discharged its contents onto the floor. So poor were the safety measures, that dust was even found in the canteens provided by the company. In the tanks used for curing the products an absence of ladders and suitable platforms for the operatives made for a considerable danger of falling, while in the crushing mill the noise was extraordinary and affected the workers. Some of the belting driving the machinery was not provided with safety guards. Cracks in the wall of a shed used for carborundum cutting wheels suggested that this building was quite unsafe. In this works there was no doctor and no care was taken to secure regular examination of the staff. No individual charged with safety and health measures could be found. The authors made such detailed and such numerous recommendations for improvements that they can only be mentioned. Until two years ago no safety or health precautions of any kind were taken in this factory. *G. C. Pether.*

HUREL, J. Contribution à l'étude de l'asbestose. **[A Contribution to the Study of Asbestosis]** *Arch. Méd.-Chirurg. de Normandie.* 1960, May & June–July, v. 51, Nos. 98 & 99 (n.s.), 381–407; 463–93. [41 refs.]

The chief interest in this paper is in the 11 cases of asbestosis recorded. 3 of these were severe, the others moderate or minimal. In one of the minimal cases the disease appeared after only 5 years' exposure to asbestos dust. Some of the subjects had been employed in parts of the factory where the dust content of the air was less than that allowed in Canada, namely 176 particles per cc.; a better standard is therefore required. Some of the cases, too, were undoubtedly produced by small particles, usually from 3 to 5 microns.

One of the men had pulmonary tuberculosis and later a carcinoma appeared. In most cases the results of various respiratory function tests are given. In the moderate and minimal disease the results varied considerably; in severe disease they confirmed the extreme functional disturbance. Although an alveolar capillary block was suspected, it could not be confirmed by the tests used. *Charles L. Sutherland*

KEAL, E. E. **Asbestosis and Abdominal Neoplasms.** *Lancet.* 1960, Dec. 3, 1211–16, 8 figs. [25 refs.]

In 1953 the impression was formed at the London Hospital that women suffering from pulmonary asbestosis had ovarian neoplasms more often than other women. Accordingly a search of the hospital records from 1948 was made. This revealed that 23 women suffering from asbestosis had been treated as in-patients. 15 are known to have died, 4 with lung cancer and 9 with intra-abdominal neoplasms. Of these 9, 1 had an ovarian carcinoma, 4 had peritoneal growths possibly of ovarian origin, and in the remaining 4 the diagnosis was carcinomatosis peritonei. Detailed case histories of the 9 cases are tabulated. The author records that he is not able to advance any single satisfactory explanation to cover these findings but submits that they appear to form a clinical entity of statistical significance.

[The literature on cancer—lung, pleura and other organs—associated with asbestosis is increasing. The statistics in Great Britain, however, are vitiated by the fact that several of the series usually cited and on which estimates of incidence are made comprise the same cases. Since 1947 the Senior Medical Inspector of Factories has periodically reviewed the cases collected by the department in the Annual Report of the Chief Inspector of Factories. This is the most comprehensive source of data in the United Kingdom and should be used as a base-line.] *A. Meiklejohn*

MINISTRY OF PENSIONS & NATIONAL INSURANCE. **National Insurance (Industrial Injuries) Act, 1946. Byssinosis. Review of Occupational Cover: Cotton-Spinners. Review by the Industrial Injuries Advisory Council** [PLANT, A., Chairman] **in accordance with Section 61 of the National Insurance (Industrial Injuries) Act, 1946, of the Occupational Cover in respect of Byssinosis within the Cotton Industry.** Cmnd. 1095. 11 pp. 1960. London: H.M. Stationery Office. [9d.]

The occupational cover for byssinosis in the cotton industry in Britain has been reviewed. After further surveys, it is concluded that:—

(1) There is no case for extending insurance cover to ring room workers. Out of some 400 ring spinners working in 3 mills, 10 had symptoms of byssinosis. The only spinner with disabling byssinosis had previously worked for 16 years in a card room.

(2) Out of 351 mule room workers aged 40 years and over, at work in 7 mills, 10 had symptoms of byssinosis. Two were disabled by the disease. In a group of 40 mule spinners selected for investigation by their trade union because they were disabled by breathlessness, 2 had byssinosis and in one the condition was thought to be disabling.

Although there is evidence that disabling byssinosis does occur in mule room workers, the report states that the evidence does not warrant extending insurance cover to them.

For the cotton operatives, the one encouraging feature of this report is that arrangements have been made between the trade union and the Nuffield Department of Occupational Health to investigate workers in whom disabling byssinosis is suspected. *R. S. F. Schilling*

BUECHNER, H. A. **Bagassosis. Peculiarities of its Geographical Pattern and Report of the First Case from Peru and Puerto Rico.** *J. Amer. Med. Ass.* 1960, Nov. 5, v. 174, No. 10, 1237–41, 2 figs. [15 refs.]

The author reviews recent reports on bagassosis showing that it is an occupational pulmonary disease of increasing importance. It occurs in many countries where dried bagasse or sugar-cane fibre is handled. Few if any cases have resulted from contact with fresh sugar cane or moist bagasse. This explains why the disease has been reported in only 4 out of 60 factories in Louisiana handling bagasse. Bagassosis has recently appeared at a newly-established paper mill in Puerto Rico where approximately 80 cases have been observed. The first of these is described in detail. *R. S. F. Schilling*

UNITED STATES DEPT. HEALTH, EDUCATION & WELFARE. **Public Health Aspects of Increasing Tetraethyl Lead Content in Motor Fuel. A Report: Advisory Committee on Tetraethyl Lead** [MAGNUSON, H. J., Chairman] **to Surgeon General of Public Health Service.** *Pub. Health Service Publication No. 712.* 1959. pp. ix + 49, 9 figs. Wash. 25, D.C.: Superintendent of Documents, U. S. Govt. Printing Office. [$0.30.]

This is the Report of an expert Advisory Committee convened by the Surgeon General of the Public Health Service in January 1959 in "response to the expressed interest of the petroleum industry in increasing the tetraethyl lead content in motor fuel". In the preface it is stated "Since the Public Health Service has no legal authority to control the concentration of lead in gasoline, the committee's findings should not be interpreted as a regulation of the Public Health Service or as an agreement with the industry".

The Report is well presented and contains a large amount of interesting and valuable information. The annual domestic consumption of tetraethyl lead (TEL) in the United States has increased from 700,000 pounds in 1924 to a maximum of 5·1 million pounds in 1956 and further increase is projected by the industry. Particulars of this usage are presented in tables and figures which are followed by a short section of the report on health and environmental data on atmospheric lead concentration.

Much of the Report is devoted to the technical aspects of the proposed increases of TEL additions with mention of studies carried out at the Ethyl Corporation Research Laboratories. The conclusion reached is that an increase of TEL concentration above the present limit of 3 ml. per gallon of fuel to 4 ml. "will have a favorable effect on the national economy without creating a public health hazard or a technical problem in the areas discussed herein."

Under the heading of "Hygienic Aspects" there is

an abstract of a statement from the Medical Consultant to the Ethyl Corporation which is to be published in full by the Kettering Laboratory of the University of Cincinnati.

In its conclusions the Committee " wishes to point out that a conclusive answer is impossible at the present time because of the lack of medical data ". Investigations of such matters as " body lead burdens " were recommended by the Surgeon General's Committee in 1926 but regrettably were not carried out by the Public Health Service.

Nevertheless the conclusions of the present Committee about the projected increase in TEL concentration were " that (1) a change in the maximum tetraethyl lead in motor fuel from 3·0 to 4·0 cc. would not increase the hazards involved in the manufacture and distribution of leaded gasoline and (2) available data do not indicate that such change would significantly increase the hazard to public health from air pollution ". *M. E. Delafield*

BAETJER, A. M., JOARDAR, S. N. D. & MCQUARY, W. A. **Effect of Environmental Temperature and Humidity on Lead Poisoning in Animals.** *Arch. Environment. Health.* Chicago. 1960, Dec., v. 1, No. 6, 463–77, 6 charts. [24 refs.]

In mice acutely and chronically poisoned by Pb, mortality rates, latent periods and survival times were compared for variable exposures to temperatures of 95°, 72° or 60° F. Comparisons were also made under conditions simulating physiological effects of heat: dehydration; increased metabolism from thyroxine; decreased activity. Results were confirmed in rats. In most of the many experiments approximate LD50 values of Pb acetate or Pb nitrate were injected. Precipitation of Pb in the peritoneum from the acetate was prevented. Controls received the Na salts. Humidity in the normal and cold chambers was generally 50% and in the hot chamber 85%, 25% or 95%. For excretion experiments rats were intravenously injected with smaller doses, 1 or 1·5 mgm. Pb per 100 gm.

When acutely poisoned by Pb intravenously or intraperitoneally, mice at 95° F began to die sooner, had a higher mortality rate and survived for shorter times than at 72°. Rate of absorption made no difference. Effects were more marked when there had been no exposure to heat before poisoning, but prolonging exposure beforehand to achieve acclimatization did not reduce harmful effects. Removal from the hot chamber at night alleviated the effects to some extent. High or low humidity did not affect results. Mice with chronic poisoning began to die sooner and had a higher mortality at the high temperature. The cold environment produced a higher mortality and longer survival than 72° after the intraperitoneal injections but not after intravenous administration.

Dehydration, at all temperatures, increased mortality from acute poisoning, especially after intraperitoneal injection. At normal temperatures, susceptibility to poisoning was not affected by weight loss or decreased activity, but it was, in female mice, by thyroxine. Less Pb was excreted in urine and faeces by rats exposed to 95° than by those at normal and cold temperatures. [See also this *Bulletin*, 1959, v. 34, 785.]

M. Patricia Fitzsimons

KING, E. & THOMPSON, A. R. **Relative Significance of Tests for Industrial Lead Absorption and Poisoning determined by Field Surveys.** *Indust. Med. & Surgery.* Miami. 1960, Nov., v. 29, No. 11, 534–9, 10 figs.

Whether the criterion is to assess Pb absorption or plumbism, *i.e.* cause or effect, evidence of the former calls for environmental control. This 3 months' survey (at Luton, England) shows the relationships between 540 sets of data where there was a wide range of atmospheric Pb concentrations. Techniques, not necessarily the most desirable academically, were such as could be used in any factory.

There were 491 men working in low concentrations, 70 having clinical signs; 34 in high concentrations, 17 having signs; and 15 not working because of obvious signs of excessive exposure. In each category, a table shows the percentages of men with more than: a trace of coproporphyrin, 80 μgm. Pb per 100 ml. blood, 150 μgm. Pb per litre urine, and 1 and 3 stippled cells per 1,000 red blood cells; and of men with less than 80% haemoglobin (Hb). Excepting the 15 ill men, the only group difference in laboratory findings between clinically positive and negative subjects was the blood Pb. Also, the percentage with high blood Pb was not any higher among 25 men graded with the more severe clinical effects among the 70 mentioned above. The tests gave an indication of exposure rather than of clinical effects.

Several series of histograms compare various levels of laboratory estimations—each level with others of its own kind and with other estimations and clinical gradings. Though there was some direct relationship with blood Pb and other criteria, it was possible to have a high blood Pb and low urinary Pb and punctate count, and the reverse. Apart from men with very low haemoglobin (Hb), there was little agreement between Hb values and other criteria. Punctate basophilia gave poor agreement, except for higher counts. Urinary Pb showed good agreement with coproporphyrin data. Clinical grading agreed only loosely with laboratory results except at high levels—apart from Hb values which, in any case, were assessable on clinical examination. The full complement of laboratory tests when graded agreed more with clinical assessments than did each kind of test.

Although the results suggests no single answer for judging the relative merits of criteria for planning control policy, a policy whereby any positive findings for the chosen criteria are followed by engineering control will be successful. Smaller factories may find the positive semi-quantitative coproporphyrin test of value if applied to the whole group and not only to the individual.

M. Patricia Fitzsimons

JACOBS, M. B., YAMAGUCHI, S., GOLDWATER, L. J. & GILBERT, H. **Determination of Mercury in Blood.** *Amer. Indust. Hyg. Ass. J.* 1960, Dec., v. 21, No. 6, 475–80, 4 figs. [36 refs.]

" A method for the ultramicro-determination of mercury in blood has been presented. It depends upon a

cold digestion of the blood with potassium permanganate and sulfuric acid, separation of the mercury by a dithizone extraction, liberation of mercury vapor by the destructive distillation of the mercury dithizonate, and estimation of the mercury by use of an ultraviolet light mercury vapor meter. Only one milliliter of blood is required for a determination. The method is suitable for the milli- and centimicrogram range, that is for 10^{-8} to 10^{-9} gram of mercury."

PERNIS, B., VIGLIANI, E. C., CAVAGNA, G. & FINULLI, M. **Endogenous Pyrogen in the Pathogenesis of Zinc-Fume Fever.** *Med. d. Lavoro.* 1960, Oct., v. 51, No. 10, 579–86, 7 figs. [14 refs.]

On the hypothesis that zinc-fume fever may be caused by endogenous pyrogen liberated from leucocytes in the lung by the direct action of ZnO fume, these experiments were modelled on the work on pyrogens induced by endotoxins and viruses [ATKINS and WOOD, *J. Exper. Med.*, 1955, v. 101, 519; v. 102, 499; this *Bulletin*, 1955, v. 30 (805); 1956, v. 31 (325); ATKINS and HUANG, *ibid.*, 1958, v. 33, 620 *bis*]. Failure before this to cause fever in animals exposed to ZnO fume was overcome by pre-treatment with an irritant gas.

Untreated rabbits were exposed for 30 mintues to ZnO fume equivalent to 500–600 mgm. Zn per m^3. Rectal temperatures fell. Circulating leucocytes increased. Other rabbits inhaled a 20% acetic acid aerosol for 10 minutes. Coughing and dyspnoea followed but no pyrexia. When rabbits inhaled this aerosol, 16 hours and 1 hour before being exposed to the fume, rectal temperatures increased for 12 hours, starting after a latent period of 5–6 hours, comparable with clinical experience. Also, acquired tolerance, which occurs in men, was reproduced in rabbits after inhaling aerosol and fume on 2 or more consecutive days. On the other hand, cross-tolerance between metal-fume fever and endotoxin did not develop: tolerance to endotoxin by daily intravenous injections of increasing doses of *Salmonella abortus equi* lipopolysaccharide was achieved, with only slight increase of temperature after the final large dose, but these rabbits had a typical ZnO fever curve when exposed as above on the following day. Metal-fume fever, therefore, was not due to bacterial or endotoxin-like endogenous pyrogen. Serum taken from rabbits during fume fever caused an immediate increase of temperature when injected into normal rabbits; transfer from controls did not. This demonstrated, by the characteristic transfer peak, that an endogenous pyrogen had been present in the blood of the experimental animals. Fever was also induced in rabbits by injection of ZnO fume in saline.

Lung capillaries are shown filled with leucocytes in aerosol-treated rabbits killed immediately after exposure to ZnO fume. The latent period may be due to the time necessary for leucocytes to collect or for ZnO particles, shown under the electron microscope, to pass through alveolar walls. Injection of influenza virus causes in the rabbit a similar latent period and rapid tolerance after a second dose [this *Bulletin*, 1958, v. 33, 620, *ter*].

M. Patricia Fitzsimons

BERLIN, M. & FRIBERG, L. **Bone-Marrow Activity and Erythrocyte Destruction in Chronic Cadmium Poisoning, Studies with Fe^{59} on Rabbits.** *Arch. Environment. Health.* Chicago. 1960, Dec., v. 1, No. 6, 478–86, 5 figs. [24 refs.]

The life span of labelled erythrocytes and the course of blood estimations are shown in figures; experimental and statistical methods are described. The radioactivity of the blood was measured for 9 weeks in 3 groups of rabbits after an intravenous injection of 6μC of $^{59}FeCl_3$, specific activity 3·25 mC per mgm. To inhibit re-uptake of iron from destroyed erythrocytes, this was followed 7 days later by intramuscular injections of 100 mgm. of non-radioactive iron. This improved anaemia in all groups, the controls, Group III, having developed slight nutritional anaemia. Group I, for 6 weeks before the isotope, was injected subcutaneously with cadmium chloride, 1 mgm. Cd per kgm. each day on 6 days a week, and afterwards with halved doses every 3 days for 9 weeks. Group II had whole doses from the 7th day after the isotope. Group I developed anaemia before the isotope, Group II afterwards but less severely. The hypochromic, microcytic anaemia became normocytic after the non-radioactive iron but the haemoglobin did not reach pre-experiment levels, as it did in controls. Erythrocyte resistance was not altered.

The ^{59}Fe content of the blood, as percentages of the injected amounts, is shown in curves. There are 2 curves for each Cd group because the blood volume was calculated by 2 methods. Tagged erythrocytes appeared sooner in Groups I and II—suggesting increased marrow activity—and decreased more rapidly than in Group III. The content 60 days after the isotope was about 20%, 10% and 40% in Groups I, II and III respectively. The 2 curves for Group II were closely above and below the controls' normal curve for 30–40 days and then rapidly fell. Accelerated destruction of erythrocytes and deficiency of iron in the marrow contributed to the anaemia of Cd poisoning. *M. Patricia Fitzsimons*

MACFARLAND, H. N. **The Use of Dimercaprol (BAL) in the Treatment of Cadmium Oxide Fume Poisoning.** *Arch. Environment. Health.* Chicago. 1960, Dec., v. 1, No. 6, 487–96, 5 figs. [44 refs.]

These experiments show that BAL reduced mortality and prolonged survival in acute poisoning from cadmium oxide fume. Inhalation of arc-produced fume for 15 minutes caused 20%, 50%, 70% and 90% of 200 gm. rats to die at concentrations of 34, 46·1, 52·6 and 63·7 μgm. CdO per litre respectively. Analysis by the probit technique gave an L(Ct)50 of 666 mgm. minute per m^3 and an L(Ct)95 of 1088.

In 3 factorially-designed experiments, after 126, 210 and 162 rats inhaled respectively 4·25, 4·5 and 3·1 times the L(Ct)95, BAL was administered subcutaneously among the trial groups as follows: first trial, once, twice or 4 times daily for 5½ days at levels of 12, 24 or 48 mgm. per kgm.; second, 2, 4, 6 or 8 times in 1 day at 12, 36 or 108 mgm. per rat; third, 3, 6 or 9 times in 1 day at 7·2, 14·4 or 21·6 mgm. per rat.

Nearly complete protection resulted from approximately 100 mgm. BAL in divided doses. In the first trial, over 60% survived in the best group, at 9·6 mgm. per 200 gm. rat given every 6 hours; over the above range of amounts and frequencies, protection increased with an increase in both these factors; survivors lived longer than controls. In the second, 12 mgm. per rat every 4 hours gave complete protection and this dose at the other frequencies gave high protection and so did 36 mgm. every 12 hours; higher doses and frequencies were ineffective, probably toxic. The third trial confirmed the efficacy of BAL: at 7·2 mgm. survivors increased with increasing frequencies of dose, at 21·6 the reverse held, and the middle dose gave maximum protection at the middle frequency.

Reasons are given why renal damage may be negligible after inhalation treated by BAL: the differences between acute and chronic poisoning, between CdO fume and experimental aqueous Cd chloride aerosol and between inhalation and other experimental administration. Reconsideration of clinical use of BAL for acute CdO fume poisoning is recommended. *M. Patricia Fitzsimons*

BELTH, S. M., KAPLAN, E. & COUCHMAN, C. E. **The Collection and Determination of Chromium in an Urban Atmosphere.** *Arch. Environment. Health.* Chicago. 1960, Oct., v. 1, No. 4, 311–15, 3 figs.

The method is described in detail and can be used in large numbers of atmospheric dust samples for determinations in the range of 0 to 10 μgm. CrO_3 (0 to 5·2 μgm. Cr). During July and August 1959 in Baltimore samples were obtained on filter paper tape during 2-hour intervals by an automatic smoke sampler. Each week the tape with its 84 1-inch dust spots was submitted for analysis. Samples cut from the tape and identified by time were dry-ashed in Pyrex tubes standing in an aluminium furnace-rack, fused with sodium peroxide, leached with water, acidified and treated with s-diphenylcarbazide. The colour was matched against freshly prepared standards. Values were for total Cr. Interference and possible contamination are discussed.

A figure shows wind directions plotted against concentrations and the number of samples. Maximum concentrations appeared when the wind came from the direction of a chrome chemical processing plant some 700 ft. south-east of the sampling station. Another shows average and peak concentrations, which are parallel, for each 2-hour period of 1 day. They were highest in the afternoon and lowest in the 2 hours before major operations began in the plant each morning. Concentrations rose quickly after this but after the day's work decreased gradually.

There was a background level of Cr of the order of 0·88 μgm. CrO_3 per sample. This was equivalent to 60×10^{-3} μgm. Cr per m^3, reasonably close to the average Cr concentration of 70×10^{-3} μgm. per m^3 reported for the 1957 network for the Baltimore Station.

M. Patricia Fitzsimons

NAGAI, I. **[An Experimental Study of Selenium Poisoning]** *Igaku Kenkyu.* Fukuoka. 1959, May, v. 29, No. 5, 1505–32, 5 figs. & 27 charts. [52 refs.] [In Japanese.]

The English summary appended to the paper is as follows:—

"No small proportions of the workers employed in the medium and small enterprises are minors and women who are, as a general rule, highly susceptible to a variety of occupational diseases, to factory-caused poisoning of different sorts, in particular.

"The author inspected from a hygienic point of view the workers engaged in the manufacture of selenium rectifiers in a certain factory and carried out, on the other hand, an experimental study of selenium poisoning in animals.

Result

"1) A long service in the factory was likely to cause hypochromic anemia in the workers, producing in them first a characteristic variation and finally a drastic reduction in the number of leucocytes.

"2) The old belief, that the finger-nails are readily affected by selenium, was not unconditionally acceptable, according to the subjective complaints brought by the workers for the author's investigation. The nails found damaged were those brought in frequent contact with selenium, showing that the substance does not select the nail as the object of its attack.

"3) In the case of female workers, irregular menses and menostasis occurring in an increasing number of cases appeared more or less ascribable to the toxic action of selenium.

"4) Animal experiments with selenium showed that selenium poisoning, either acute or chronic, prolonged the sexual cycle in the animals used and inhibited their sexual activity, and that the females were affected more severely than the males."

PRIOR, J. T., CRONK, G. A. & ZIEGLER, D. D. **Pathological Changes associated with the Inhalation of Sodium Zirconium Lactate.** *Arch. Environment. Health.* Chicago. 1960, Oct., v. 1, No. 4, 297–300, 6 figs.

Rabbits weighing 1,500–2,000 gm. were exposed during 20 minutes each day for 6 weeks to a mist obtained by atomizing 0·48 ml. of a 44% aqueous solution of sodium zirconium lactate into a box of 9,204 cc. capacity, every 5 minutes. The concentration was approximately 0·049 mgm. per cc. During exposure there was no evidence of irritation. Material from the mist settled on the fur and was licked. Survivors of the 6 test animals (number not stated) were killed. All 6 controls remained healthy and showed no histological evidence of infections or granulomas. Some animals had had intra- or subcutaneous injections of zirconium salts 4 months previously.

All test animals had either visible upper lobe nodules which were bronchiolar abscesses surrounded by connective tissue and pneumonia or peribronchial granulomas. The latter were not encapsuled and were composed of round masses or diffuse arrangements of histiocytes which contained a brown granular substance, suspected to be stained zirconium; this is being investigated. Terminal bronchioles showed squamous metaplasia. The liver in most animals had a black granular appearance. Microscopy showed pale swollen cells with some nuclear irregularity. A granuloma was found in the tongue of

1 animal, a recent gastric ulcer in another, and marrow emboli in the lungs of another. Some animals had tracheitis and nasal sinus inflammation.

M. Patricia Fitzsimons

CRUICKSHANK, C. N. D. **The Use of Tissue Cultures for Toxicity Tests.** *Trans. Ass. Indust. Med. Officers.* 1960, Oct., v. 10, No. 3, 94–6, 3 figs.

This brief sketch is illustrated by results found when testing tributylin by some of the simplified techniques used for assessing the toxicity of new chemicals in the Medical Research Council unit for experimental pathology of the skin. Photographs of sections of 3-day cultures of guineapig skin show the normal encysted appearance and the destruction of tissue and absence of epidermal cell migration which developed after a specimen had been floated on the medium to which 1 in 50,000 tributylin had been added. A figure compares against acetone as standard the inhibition of the respiration rate of skin slices produced by 4 concentrations of tributylin oxide in acetone. By a similar test equivalent inhibition was caused in 24 hours by 1 in 50,000 tributylin and by 1 in 1,000 turpentine. However, *in vivo* tests on guineapigs' flanks showed it to be 1,000 times more toxic than undiluted turpentine which caused no erythema: the tributylin, 1 in 1,000, caused erythema, possibly being absorbed.

Tissue culture is useful with materials which have a non-specific poisonous effect on all cells. It is no alternative to animal experimentation for determining effects of ingestion or inhalation. Results should be interpreted with caution; materials which are non-toxic *in vitro* may be transformed in the living organism to toxic metabolites. When toxic to cells *in vitro*, chemicals can usually be regarded as toxic *in vivo*, though not necessarily at the same concentrations, higher concentrations being required to produce ill effects *in vivo*. [See also this *Bulletin*, 1953, v. 28, 277.] *M. Patricia Fitzsimons*

FEDERATION PROC. Wash. 1960, Sept., v. 19, No. 3, Pt. 2, Suppl. No. 4, pp. iv + 52, 5 figs. [Numerous refs.] **Proceedings of a Symposium on Problems in Toxicology held in Chicago, Illinois, April 13, 1960** [COON, J. M. & MAYNARD, E. A. (Edited by)].

This valuable and interesting symposium of papers on modern problems in toxicology was sponsored by the American Society for Pharmacology and Experimental Therapeutics and the American Institute of Nutrition and organized by committees of the National Research Council and the Toxicology Study Section of the National Institutes of Health.

The Chairman of the Morning Session of the Proceedings (Chauncey D. LEAKE) referred shortly to the various problems of "social toxicology" which may arise through the variety and extent of man's use of potentially toxic chemicals in industry and pest control; the addition of chemicals to food, radiation hazards and the increasing number of drugs that are being employed in "a terrifying way".

The *Introduction* (R. K. CANNAN, pp. 1–2) contains an expansion of the Chairman's remarks and the statement that in the past 20 years the output "in millions of pounds per annum" of pesticides has increased from 8 to 540, of plastics from 150 to 5,000 and of detergents from 15 to 3,000. Also that in the present year we may expect some 10,000 new compounds to become available in commercial quantities.

Our man-made noxious environment (E. M. K. GEILING and W. D'AQUANNO, pp. 3–9). The authors say "We cannot minimize the seriousness of the existing hazards, nor is control of the existing hazards impossible". Sections of this paper deal with: (1) radiation hazards with mention of the fact that there is "enough radioactive waste material in huge steel tanks at five different locations in the United States to cause severe pollution of all the land and water areas of the country", (2) accidental poisonings which in the United States caused 1,429 deaths in 1958 and the setting up of Poison Control Centers, (3) the organizing of an "Adverse Reaction Reporting Program (ARRP) for the reporting of unusual or adverse reactions to drugs", and (5) drugs and antibiotics used in animal feeds (itemized in tables) for prophylactic and therapeutic purposes and to increase the efficiency of food utilization. Residues of some of these may appear in the meat and in milk. Short descriptions are also given of chemicals used in food processing and of air and water pollution.

Food: additives and natural components (W. J. DARBY, pp. 10–12). This is a short but interesting paper in which examples are given of nutrients which "may be unique either in the relatively small margin of safety between beneficial level and toxic level or the ease with which grossly excessive quantities can be ingested under unusual conditions". Examples of the small safety margin exist in the substances iodine, fluorine and selenium. Examples of gross overdosage causing illness in man or animals or both are mentioned for hypervitaminosis and cobalt, riboflavin, lactose and certain amino acids. The "toxicity of excess" NaCl is also described. Apart from this many foods when taken in excess produce recognized syndromes or pharmacological effects in man. Among the quoted examples of these are antitrypsin in uncooked soya, phytate in cereals, oxalate in rhubarb and spinach, saponins in many foods and goitrogens in foods. Many syndromes are caused by food toxins: lathyrism, epidemic dropsy caused by argemone oil, fagopyrism (the photosensitization induced by buckwheat), shellfish poisoning and the like.

Control of toxicity in foods, drugs and cosmetics (A. J. LEHMAN, pp. 13–16). This is an account of the working, value in control and difficulties of the Food Additives Amendment 1958, the Federal Food, Drug and Cosmetic Act, 1938, and the Skin Toxicity Branch of the Food and Drug Administration. There is some description of the constituents of preparations used for hair-waving, hair dyeing, depilation or as antiperspirants and deodorants which are tested for toxicity.

Agricultural chemicals (G. C. DECKER, pp. 17–21). In this paper the more practical problems involved in the use of agricultural chemicals are considered from the viewpoint of an entomologist. These problems are discussed in their different aspects with many references to the literature. The view is expressed that "Today

all experts who know whereof they speak, whether they be agriculturists or public health officials, recognize pesticides as weapons essential to man's continued success in his battle for survival".

Chemicals in industry (H. W. GERARDE, pp. 22–25). This is a short paper in which there is a discussion of the role which the industrial toxicologist plays in the commercial development of chemicals. In the introductory remarks there is reference to the explosive growth in the production of chemicals in the past 10–20 years and to the estimate that 50,000 new chemicals will be synthesized during 1960.

Water and atmosphere (H. E. STOKINGER, pp. 26–30). The major research problems in water and air which are the result of modern industrial and other activities are described under the headings of: (1) chemical synthetics, (2) increasing mineralization and (3) lifetime effects of trace substances in water, and (4) toxicological problems associated with air pollution.

In the Afternoon Session of the Proceedings the Chairman (W. H. SEBRELL, Jr.) in his introductory remarks (pp. 31–32) referred to the fact that although "assailed from all directions by a multitude of toxic substances" nevertheless the United States has excellent health and much of this is due "to the thousands of new chemical compounds which are an essential part of our health and prosperity".

Radioactive materials (C. L. DUNHAM, pp. 33–35). A short interesting paper mainly on biological effects of radiation with the conclusion that "we must develop in the very near future an intelligent understanding of the hazards of the ionizing radiations, the automobile, atmospheric pollutants, water pollutants, food additives and insecticides. We must put each one in its place—in proper perspective and under appropriate controls".

Some toxicological hazards in submarines (J. L. KINSEY, pp. 36–39). This paper contains outlines of some of the techniques and equipment currently being used in a nuclear-powered submarine to "purify" the atmosphere, with a discussion of some specific problems which exist in submarine life.

Space hazards (D. E. SMITH, pp. 40–42). Much of this short paper is devoted to some description of recent work on the Van Allen radiation belts around the earth and on cosmic rays, with mention of other space hazards which arise from the contents of the space vehicle and the external environment.

Recognition of toxicology as a scientific discipline (H. F. SMYTH, Jr., pp. 43–49). In this paper the author discusses the shortcomings and difficulties of pharmacological research and says "New viewpoints, new knowledge and new data are needed to replace some of our pragmatic activities with truly scientific operations".

Training of toxicologists (H. C. HODGE, pp. 50–52). This is in the main a short account of the urgent needs for the education of toxicologists whose training at present is not adequate. *M. E. Delafield*

CIRLA, P. La sostituzione del benzolo con eptano (studio clinico). [**Substitution of Benzol by Heptane. Clinical Study**] *Rass. Med. Indust.* Rome. 1960, July–Aug., v. 29, No. 4, 276–87. [19 refs.] English summary.

While the literature on the toxic effects of benzol is almost mountainous and many articles have been written about its possible substitution by less toxic solvents, the author points out that extremely little is known about the toxicity of a recently proposed substitute—heptane, the MAC of which is put at between 300 and 500 p.p.m.

He therefore examined workers in a tyre factory where ambient conditions were good and where heptane was used as a benzol substitute at almost all stages including making the various solutions, spreading them, and cleaning.

531 workers (382 men, and 149 women) aged between 21–39 for men and 23–55 for women were repeatedly examined clinically, and also had chest X-rays and blood and laboratory examinations carried out, while 50 had liver function tests performed as well.

7 men and 7 women had suggestive symptoms of headache and asthenia, some had dyspepsia; in addition 31 had gastro-duodenal ulceration and 68 disease of the liver or gall bladder. Nothing suggesting any toxic action of heptane was found in the chest but pruritus and erythema occurred in a few cases which passed off after the workers had become acclimatized. The most important condition found was anaemia, most marked in the female employees. In none were the red cells less than 3·6 million per cmm.; 10% of the women had Hb less than 80%, and there was some aniso- and poikilo-cytosis.

The author considers therefore that as slight anaemia was found in 46% of the women, it must be concluded that heptane has some toxic action on the blood-forming organs especially in older women though this is slight and in any case is many times less than for benzol. He therefore considers that heptane can be regarded as a satisfactory substitute for benzol.

[None of the workers had had more than 4 years' service.] *W. K. Dunscombe*

LOB, M. L'action du trichlorethylene sur le taux d'alcool dans le sang. [**Influence of Trichloroethylene on the Blood Alcohol Level**] *Med. d. Lavoro.* 1960, Oct., v. 51, No. 10, 587–92, 2 figs. [13 refs.]

Results of preliminary experiments with single doses are given after a review of the few studies that have been reported on the effect this particular solvent has on blood alcohol, a question sometimes of medico-legal interest. An *in vitro* test first, with one of its metabolites, showed by the Nicloux-Rochat method that 1 gm. trichloroethanol per litre [$^0/_{00}$ in text] in blood can increase the apparent blood alcohol concentration by 0·18 gm. per litre and that 6 gm. per litre caused an error of 1 gm. per litre. By another method it had no influence.

When the author inhaled 400 p.p.m. trichloroethylene for 45 minutes and then drank 0·1 litre of whisky 15 minutes later, his blood alcohol curve is shown to be the same as after the whisky alone a few days previously.

Tables give serial estimations of blood alcohol for 150 minutes in control rabbits intravenously injected with 1·3 cc. alcohol per kgm., diluted to 10cc., and in others injected intravenously with 10 mgm. trichloroethylene per kgm., diluted, 10 minutes before the alcohol and in others injected with both substances simultaneously. Mean

results gave similar curves; blood alcohol after 10 minutes was between 1·5 and 1·6 gm. per litre and descended to 0·7 in control and experimental animals. Intravenous injection of 30 or 120 mgm. trichloroethylene per kgm. in 2 rabbits did not influence the alcohol reaction. *M. Patricia Fitzsimons*

LINIECKI, J. **The Effect of Chronic Carbon Disulphide Poisoning on Thiamine Balance in Rats.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 2, 212–22, 4 figs. [23 refs.]

Because one of the theories to explain the development of nervous system changes in CS_2 poisoning has been based on a toxic deficiency of vitamin B1 [this *Bulletin*, 1942, v. 17, 160], the aim of this work was to determine whether CS_2 poisoning resulted in depletion of the vitamin. Groups of 8 rats, A, B and C, were given a diet containing 40 μgm. thiamine daily for each rat, 2·5–4 times the normal requirement, throughout the 24-week experiment. After 6 weeks on the diet, A and B were exposed for 129 days for 1·5 hours daily on 6 days a week to 0·425 and 1·55 p.p.m. CS_2 respectively. Figures show daily excretion of thiamine in urine and faeces, and daily urinary excretion of N-methylnicotinamide, with regression lines, and tables give mean values of these and other results. Saturation tests were performed by injecting 100 μgm. thiamine just before exposure and 99 days later.

Group B developed severe chronic CS_2 poisoning, with loss of weight, paresis or paralysis of limbs and lengthening of motor chronaxia. The brain weighed 18% less than in group C and contained 21% more thiamine. In the liver there was only 15% less thiamine. Urinary excretion of thiamine between the 28th and 99th day of exposure remained constant and was decreased by only 17% when compared with C values, this figure being reduced to 12% when B's lessened food intake was accounted for. The saturation tests showed no significant changes in any group, and faecal excretion of thiamine was similar in all groups. Early nervous system lesions —lengthening of flexor chronaxia—were seen in A, but no changes in thiamine balance.

The mean excretion of N-methylnicotinamide between the 28th and 122nd days of exposure was: A, 76 μgm. per rat per day; B, 133·8; and C, 80·7. The increased excretion by B seemed proof of disturbed nicotinic acid metabolism, possibly in enzyme protein. The results of the experiment showed no evidence of B1 hypovitaminosis, which could not, therefore, account for the nervous system changes. *M. Patricia Fitzsimons*

HENDERSON, Maureen & APTHORP, G. H. **Rapid Method for Estimation of Carbon Monoxide in Blood.** *Brit. Med. J.* 1960, Dec. 24, 1853–4, 3 figs.

The method described is based on SJÖSTRAND'S method [*Acta. Physiol. Scandinavica*, 1948, v. 16, 201] but is quicker. To try it out 6 subjects were used. They first cleared their lungs of nitrogen by breathing pure oxygen for 3 minutes, and then exhaled a maximum inspiration into an empty bag, from which they then rebreathed for 3 minutes. The contents of the bag were analysed for oxygen (O_2) and carbon monoxide (CO), and carboxyhaemoglobin (COHb) was calculated by Dahlström's equation. During the last minute of rebreathing, venous blood was drawn, from which blood CO was also measured directly. A scatter diagram shows that the two methods agree to within about 10% and the differences seem random. A further experiment with 14 normal subjects and 32 patients with cardiac or respiratory diseases showed no significant variation of the O_2 content of the bag between the different classes of subject. Measurement of O_2 is the most laborious part of the estimation, and the authors show by another scatter diagram that an assumed value of 92% O_2 in Dahlström's equation is accurate enough for estimating COHb. No patient had any difficulty in using the method. *J. McK. Ellison*

DAVIS, A., SCHAFER, L. J. & BELL, Z. G. **The Effects on Human Volunteers of Exposure to Air containing Gasoline Vapor.** *Arch. Environment. Health.* Chicago. 1960, Dec., v. 1, No. 6, 548–54, 3 figs.

Subjective effects were noted by volunteers when exposed to low vapour concentrations of 3 kinds of non-leaded petrols, and a comparison was made between the only significant effect, eye irritation, and an objective change, conjunctival injection, as shown in coloured photographs taken before and after exposures.

Petrol A contained approximately 25% paraffins, 30% naphthenes and 40% aromatics; sample B, 40%, 35% and 20%; sample C, 30%, 5% and 65%. Each of the 10 subjects remained for 30 minutes, on different days, in an exposure chamber where the air contained a nominal concentration of 200, 500 or 1,000 p.p.m. of A, B or C. The air was changed 15 times per hour. The order of individual experiments and 2 control exposures to air was randomized.

A summary of answers to 21 questions shows relatively few positive responses to any sample. Differences in responses were related to concentrations and not to compositions. The total number of agreements between subjective irritation and objective injection were 24, 12 and 20 at 200, 500 and 1,000 p.p.m. respectively in the 30 experiments at each concentration. From each petrol at each concentration the number of instances of increased injection was: A, 3, 6, 8; B, 0, 4, 9; C, 4, 4, 7. Statistical analyses of results are given in detail and show there were no differences between petrols under these conditions; irritation and injection increased with concentrations; the former was the more sensitive indicator. *M. Patricia Fitzsimons*

TREON, J. F. & CLEVELAND, F. P. **The Physiological Response of Animals to β-Nitronaphthalene.** *Arch. Environment. Health.* Chicago. 1960, Oct., v. 1, No. 4, 324–34, 5 figs. [11 refs.]

Investigations made years ago are of interest again. They are fully described, with illustrations, *e.g.* dust

dispersing mechanism, standardization curve. β-nitronaphthalene is a yellow crystalline compound, soluble in alcohol and ether. At 15 mm. Hg it boils at 165° C.

Single oral LD50 for rabbits and rats were 2·65 and 4·4 gm. per kgm. respectively. Degenerative and necrotic lesions occurred in liver and kidney and slight degenerative changes in brain neurones. Rabbits' eyelids, conjunctivae, genital organs and urine became discoloured, pupils dilated and respiration depressed. Death took place in 1·5–4 days, and sometimes 12–16. Survivors' colour and weight became normal, but liver and kidney damage were found for 13–25 days. Methaemoglobin and Heinz bodies were formed, clotting time was increased and urine contained blood and conjugation products with sulphuric and glucuronic acids. In 2 monkeys, killed 9 and 21 days after 2·1 or 4·7 gm. per kgm., no lesions were found; vomiting and loss of weight were temporary.

Repeated oral doses of about one-tenth LD50 on 5 days each week killed 4 rabbits after 5–40 doses; 2 survived more than 100, and all 6 rats 50 doses. Findings were similar to the above, though less severe and clotting time was unaffected. Rabbits had cyanosis, distended stomachs, diarrhoea and weakness. Blood counts were normal.

Skin absorption took place when β-nitronaphthalene was applied in peanut oil to clipped intact skin in 1 dose of 9·4 gm. per kgm. for 24 hours—the rabbits developed liver and kidney damage—or in oil or water paste in repeated doses of just over 0·5 gm. per kgm. for 2 hours daily on 5 days each week for several weeks, with liver damage. The single large dose produced only local inflammation when applied as dust to abraded and intact skin. The rabbits survived all these tests, and 3 of 4 survived the repeated oil tests to abraded skin, with liver and kidney damage.

Cats, guineapigs, rats, rabbits and mice survived—with no abnormal findings—when exposed to sublimed vapour, 0·82 μgm. per litre (0·13 p.p.m.) for 7 hours daily on 5 days each week for 2 weeks, or to vapour and dust, 1·91 μgm. per litre similarly for 10 weeks. Growth rates differed little from controls', and absorption from the respiratory tract was negligible.

M. Patricia Fitzsimons

WOLFSIE, J. H. **Glycolonitrile Toxity.** *J. Occup. Med.* Chicago. 1960, Dec., v. 2, No. 12, 588–90.

Symptoms of a patient who absorbed this organic cyanide through the skin showed differences from the effects of HCN skin absorption. Onset and full recovery were slower. Another was less severely affected while driving home and recovered without treatment. Both men filled commercial 70% aqueous glycolonitrile into drums under exhaust ventilation, holding the filling line under the arm during final adjustment and capping. A leak in the line soaked their clothing. Glycolonitrile is odourless, its vapour density small and it was free from HCN used in manufacture. Shortly after finishing work, the patient developed headache, dizziness and an unsteady gait. In hospital, he only remembered walking to the works surgery, having a shower and receiving an injection. He was pale and sweating, had a rapid pulse and was still vomiting. After amyl nitrite inhalation and another shower he later became irrational and unresponsive. Oxygen remedied this only temporarily. Intravenous injection of 30 cc. 25% sodium thiosulphate was effective. He felt chilly but next day was well and returned to different work. Anorexia, nausea and vomiting recurred for a few days.

Animal experiments are reported on the basis of anhydrous $HOCH_2CN$, though dilute solutions were mostly used. The acute oral LD50 in mice was 10 mgm. per kgm. In rabbits the acute skin LD50 was between 105 and 130 mgm. per kgm.; eye instillation of 26 mgm. caused convulsions and coma in 15–30 minutes and death within 68. Inhalation of 27 p.p.m. for 8 hours killed mice and rats, but not guineapigs. Male rats showed no ill effects from ingesting 62 mgm. (females 92) per kgm. for 13 weeks; sera contained proportional thiocyanate. After intraperitoneal injection rats' sera contained cyanide and increased thiocyanate. Glycolonitrile is highly toxic—with liberation of cyanide and rapid detoxification by conversion to thiocyanate.

M. Patricia Fitzsimons

HINE, C. H., KODAMA, J. K., GUZMAN, R. J. & LOQUVAM, G. S. **The Toxicity of Allylamines.** *Arch. Environment. Health.* Chicago. 1960, Oct., v. 1, No. 4, 343–52. [16 refs.]

Monoallylamine, $CH_2=CHCH_2NH_2$ (M) and di- and triallylamine (D and T) were investigated, and also n-propylamine (P). A few of the toxicity data from some of the detailed tables are summarized here.

TEST	ANIMAL	AMINE		
		M	D	T
Single LD50, mgm./kgm.				
intragastric	mice	57	516	492
intraperitoneal		49	187	187
percutaneous	rabbits	35	356	2,250
intragastric	rats	106	578	1,310
Single LC50, p.p.m.				
exposure 1 hour	rats	1,933	7,000	3,005
4 hours		286	2,755	828
8 hours		177	795	554
Chronic inhalation (50 *7-hour exposures*)				
mortality at 20 p.p.m.	rats	0/15		
40		5/15		
100			0/15	1/15
200			5/15	6/15
			n-propylamine	
400			1/10	
Single 8-hour LC50 (n-propylamine)			2,310 p.p.m.	

M, the most toxic allylamine, especially percutaneously, is relatively more toxic than primary aliphatic amines of higher molecular weight. Additional allyl

groups decreased toxicity, though in inhalation tests this was not the case with D and T, suggesting some unrecognized property contributing to T toxicity. Orally D and T caused tremors, dyspnoea and depression. All 3 were lung, nose and eye irritants, especially M. Acute toxicity tests caused congestion of various tissues. Survivors' tissues were normal as a rule 10 days afterwards, except skin after cutaneous administration. M and D were extremely, and T mildly, irritant to eye and skin.

In chronic inhalation tests all 3 caused myocarditis; pneumonitis and some liver and kidney damage were seen. M retarded growth at 10 p.p.m. and increased the ratio of liver to body weight at 5. With D and T these changes did not occur until 200 p.p.m., though the heart enlarged at lower concentrations. Blood and marrow counts performed in the D tests were normal. The saturated propyl derivative P was much less toxic; at high fatal concentrations some animals had liver, kidney or lung damage.

Volunteers experienced eye and nose irritation, pulmonary discomfort, headache and nausea and, with T at 100 p.p.m., vertigo. By smell, M was detected at 2·5 p.p.m., D at 2 and T at 0·5. At 14 p.p.m. M was intolerable; sensory responses were not severe with D at 70 or T at 50. Protective personal equipment impervious to alkaline material is needed during work. Splashed clothing should be removed immediately to avoid burns.

M. Patricia Fitzsimons

HALSTED, H. C. **Industrial Methemoglobinemia.** *J. Occup. Med.* Chicago. 1960, Dec., v. 2, No. 12, 591–6. [17 refs.]

This review of chemical cyanosis from aromatic nitro and amino compounds includes recognition and control. Methaemoglobin (MHb), being oxidized haemoglobin, holds O_2 tightly bound, not available for tissue use. Reduction to haemoglobin (Hb) is slow. A co-existing decrease in dissociation of unaffected residual oxygenated haemoglobin increases tissue hypoxia. Hb complexes, MHb precursors, may be unidentified by conventional spectrophotometric analysis though this is satisfactory for guidance in medical control of methaemoglobinaemia.

It is usually an onlooker who first notices the characteristic blue lips: hence the advice that when leaving workers should attend for inspection of skin and nails. If no cyanosis has developed during bathing and changing, it is unlikely that serious intoxication will develop later.

Mild intoxication, MHb 15–25%, is often undetected or belittled by the subject, who may exhibit euphoria. Bed-rest and hourly blood sampling is advocated until MHb begins to decrease. Meanwhile, the history should elicit whether safety and hygiene rules had been followed —or whether accidental exposure had affected others; the skin, ears, nostrils and nails are cleansed and clothing, caps and shoes are changed again. The patient may return to work where there is no exposure, until the blood becomes normal. He should abstain from alcohol. Why it reawakens symptoms is obscure: possibly because it stimulates the oxidation mechanism, or affects reduction or liberates stored toxic compounds.

Moderate intoxication, MHb 25–50%, causes headache, vertigo, weakness, rapid pulse, marked cyanosis but rarely dyspnoea at rest. Oxygen relieves headache: it does not speed conversion of MHb but may saturate remaining Hb. Intravenous dextrose seems to hasten the normal reversible process; ascorbic acid does not and is not ideal for acute industrial methaemoglobinaemia as opposed to the familial idiopathic variety. When MHb reaches its peak it falls to normal in 24–48 hours.

Severe intoxication, MHb 50%, causes apprehension and dyspnoea. At 60–70% lethargy, convulsions and coma may develop. This medical emergency is treated by slow intravenous injection of 1% methylene blue in low dosage, 1–2 mgm. per kgm. This substance can itself form MHb, but *in vivo* is a serviceable drug for MHb detoxification, accelerating reduction. Large doses cause untoward effects. *M. Patricia Fitzsimons*

WETHERHOLD, J. M., LINCH, A. L. & CHARSHA, R. C. **Chemical Cyanosis—Causes, Effects, and Prevention.** *Arch. Environment. Health.* Chicago. 1960, Oct., v. 1, No. 4, 353–61, 8 figs. [10 refs.]

Demonstrating how blood examinations are used in environmental control during manufacture of aromatic nitro and amino compounds which cause cyanosis, this paper begins with biochemical mechanisms [see also this *Bulletin*, 1960, v. 35, 439]. Cyanosis is brought about by failure of the blood stream to deliver O_2 for vital processes. It is caused by insufficient O_2, impaired circulation or chemicals which—after absorption through lung, intestine or skin—displace O_2 or block the reaction between O_2 and haemoglobin (Hb). HbO_2 is a loose complex which dissociates easily when circulated where O_2 is demanded. In methaemoglobin (MHb) the iron has been oxidized. When Hb reacts with aromatic N derivatives the pigments are referred to as haemoglobin complexes (HbC) and the percentage difference between 2 methods of blood analysis is often, in workers exposed to the compounds, a measure of MHb precursors. A diagram shows formulae and spectrum absorption maxima of 8 HbC.

MHb or HbC values above 10% are considered abnormal, the latter indicating latent cyanosis conditions. Graphs show abnormal blood specimens in groups of potentially exposed workers preceding the onset of cyanosis. When a worker's HbC value exceeds 15%, the analysis is repeated in a few hours to determine whether metabolism is proceeding towards methaemoglobinaemia or whether detoxification mechanisms are restoring the blood to normal. Metabolism, detoxification and excretion of aniline and nitrobenzene are briefly described and the physiological effects of the anoxia associated with cyanosis. Heat and the presence of sulphides accelerate or increase cyanosis. Glucose relieves symptoms exacerbated by alcohol. Hb analyses have confirmed that injection of methylene blue results in frequent recovery.

Difficulties in prevention are discussed, and the degree to which protective equipment may be useful. Butyl rubber for routine use—accidents or heavy exposure apart—resists penetration. *M. Patricia Fitzsimons*

DE ALMEIDA, W. F. Intoxicações pelos modernos inseticidas. **[Poisoning from the Modern Insecticides]** *Rev. Paulista Med.* S. Paulo. 1959, Nov., v. 55, No. 5, 380–94. English summary.

This is a general account of toxicity levels, symptoms, treatment and prevention; it is in this sense largely a compilation. The author goes further by quoting the 55 poisonings (of which 29 were fatal) notified in the State of São Paulo in the period 1955–59; some of the subjects were children, but 46 were connected with work. Parathion was the commonest cause, and was also the most frequently used insecticide; Metasystox was next in importance.

The author ends by giving a table of maximum permissible concentrations of the various chlorinated and phosphorus compounds in mgm. per kgm. of fruits and vegetables, compiled from official sources.

[For a review of the toxicity of pesticides see this *Bulletin*, 1959, v. 34, 1205.] *Charles Wilcocks*

LACHNIT, V. & PIETSCHMANN, H. **Activity of Serum Glutamic-Oxaloacetic-Transaminase and Aldolase in Workers exposed to Halogenated Hydrocarbons.** *Indust. Med. & Surgery.* Miami. 1960, Nov., v. 29, No. 11, 523–5, 2 figs. [17 refs.]

Spectrophotometric analyses showed different values in acute poisoning by carbon tetrachloride and trichloroethylene and also as a result of an alcohol tolerance test after chronic exposure to trichloroethylene. [Though in this article methods are not described, the unit of activity was the quantity of enzyme which caused an extinction decrease of 0·001 per minute for 1 ml. serum.]

A patient vomited 10 hours after using CCl_4 for 3 hours in a well ventilated room. In hospital 3 days later the liver was enlarged and tender and there was albuminuria. The SGOT was increased by 6,000 units and aldolase by 300; GOT reached normal in 10 days, aldolase less rapidly. This paralleled the central lobular necrosis found by liver biopsy on the 8th day. By the 28th day biopsy showed little abnormality except some nuclear degeneration. His companion, 12 days after less severe exposure, had the SGOT increased to 80 and aldolase to 21; biopsy on the 22nd day showed moderate nuclear degeneration.

In 4 cases of acute trichloroethylene or tetrachloroethylene poisoning, values for both enzymes were normal except 1 SGOT value of 51 units; normal 10–33. Among 31 people chronically exposed to trichloroethylene the values were normal except that in 6 SGOT was temporarily increased by 40 units.

In people with normal liver function, not exposed to halogenated hydrocarbons, intravenous injection of 60 ml. 10% alcohol did not increase SGOT in 10 hours, nor did ingestion of 100 ml. 40% alcohol—as brandy—in 36 hours. Among 12 men and 4 women exposed to trichloroethylene, this amount of brandy after a day's work increased the SGOT 36 hours later, markedly in 6, moderately in 2, and values oscillated in the remainder; aldolase values were unchanged.

M. Patricia Fitzsimons

BELL, A. **Aldrin Poisoning: a Case Report.** *Med. J. Australia.* 1960, Oct. 29, v. 2, No. 18, 698–700, 3 figs. [13 refs.]

A labourer aged 20, in New South Wales, not previously exposed to any insecticide was engaged in emptying broken packs of aldrin into large drums and repacking it into new 5 lb. boxes. He worked for 2 successive days in a poorly ventilated shed and his skin and clothes became covered with powder. No gloves or respirator were worn. There were no washing facilities at work. At 8 p.m. on the second day while sitting quietly at home he had a convulsion. Apart from feeling sick and dizzy for about an hour he made a rapid and complete recovery. 14 days later a fat biopsy was carried out and analysis showed 40 p.p.m. dieldrin to be present.

[Aldrin is rapidly converted to dieldrin in mammalian tissues.] *J. M. Barnes*

ASHBEL, S. I., HIL, R. G. & YAVOROVSKAYA, Y. S. **[Prevention of Occupational Intoxications in Workers engaged in the Manufacture of Granozane by means of Unithiol Aerosol Inhalations]** *Gigiena Truda i Professional'nye Zabolevaniya.* Moscow. 1960, v. 4, No. 12, 16–21, 4 figs. [In Russian.]

The English summary appended to the paper is as follows:—

"Workers employed in the manufacture of the insecticide granozane are subject to the effect of diethylmercury and ethylmercurechloride, and in some sections of the industry—also to that of corrosive mercuric chloride. These compounds can penetrate the organism, circulate therein for a long time and accumulate in various organs of the body, thus leading to a pronounced occupational intoxication.

"Since, under industrial conditions, mercury compounds enter the organism chiefly via the respiratory organs and one of the principal depots thereof are the lungs,—the authors made it their task to study the possibility of resorting to aerosol inhalation of an antidote-unithiol, so as to achieve prevention of intoxication in this category of industrial workers.

"Proper inquiries helped to establish that, under the influence of such inhalations, the workers developed a considerable increase in the mercury discharge from their organism, which, to a certain degree, tends to prevent deposition of mercury compounds and serves as a prophylactic measure against mecurialism. Preventive aerosol inhalations of unithiol are well tolerated by the workers and fail to give rise to any untoward side-effects."

LOMONOVA, G. V. **[On the Toxicity of Dichloralurea]** *Gigiena Truda i Professional'nye Zabolevaniya.* Moscow. 1960, v. 4, No. 12, 27–31, 1 fig. [In Russian.]

The English summary appended to the paper is as follows:—

"Dichloralurea (DCU) is one of the new herbicides, designed for wide utilization in agricultural practice.

"To inquire into the effect produced by DCU, experiments were staged on 60 albino rats, 10 rabbits and 10 white mice. The chemical was introduced by inhalation, by way of gastro-intestinal tract and by applying it to the skin, both in acute and chronic trial tests. These proved DCU to be of but a slight toxicity, irrespective of the route chosen for its entrance into the organism of the animals cited. With DCU administered in doses of 2–3 g/kg body weight there could be noted only weakly pronounced dystrophic changes in the liver. Prolonged action of DCU in a dose of 0·5 g/kg induces an increase in the size of the thyroid, hyperplasia and hypertrophy of the follicular epithelium and an accentuated decline in the colloid amount of the follicles. Per se, DCU is unable to produce any local irritation, but, when mixed with substances capable of penetrating the skin, it tends to call forth acute dermatites in rabbits.

"The preparation is worthy of being recommended for use in agriculture."

MEDICAL RESEARCH COUNCIL. **The Hazards to Man of Nuclear and Allied Radiations. Second Report of a Committee** [HIMSWORTH, H P., Chairman] **appointed by the Medical Research Council.** Cmnd. 1225. pp. vii + 154, illustrated. [Numerous refs.] 1960. London: H.M. Stationery Office. [7s.]

Readers may well be surprised at the appearance of this Report so soon after the one of similar scope in 1956 [this *Bulletin*, 1956, v. 31, 1054], but not less appreciative on that account. The reason for it is the accumulation of new knowledge on this world-wide subject and the Committee thereby earns the gratitude of all those wishing to keep up with the present views on radiation dangers; these arise from nuclear activities and medical radiology for the most part.

There is reference in the text to the recent issue of *Radiological Hazards to Patients* (Ministry of Health, Dept. of Health for Scotland. Second Report of the Committee 1960. H.M. Stationery Office) [see below]. In this publication the Scottish Committee expressed the view that an overall reduction of the genetically effective dose from medical radiology to an annual figure of 6 mr per year would be attainable if the best techniques were always employed. It will be remembered that the tentative conclusion in the 1956 Report of the Medical Research Council was coupled with the view that a more extensive enquiry should be undertaken and this was done by the Scottish authorities [*loc. cit.*].

The general features of the present Report follow the lines of the 1956 Report with the following specific divisions: I. Introduction. II. The types of radiation and their biological effects. III. The effects of radiation on the health of the individual. IV. The genetic effects of radiation. V. Existing and foreseeable levels of exposure to radiation. VI. Assessment of the hazards of exposure to radiation.

Discussion on these matters takes up the first 50 pages and then follows a series of Appendices, A–L, from which the reader may glean the basis on which the conclusions of the Committee rest. These Appendices are written by those with first-hand observations or experiments of a world-wide character at their service.

The chief radiation danger from a fall-out appears to be that of ingestion of Strontium 90 from vegetation in the vicinity. This has assumed such importance that the Agricultural Research Council has set up its own Radiological Laboratory where any sort of food contamination by radioactive bodies can be investigated.

In general a number of concluding paragraphs to the different sections of this Report give the general impression that it confirms previous reports and this will be a great reassurance to readers.

In Australia there has been considerable doubt about the claim first made in Britain that the doses commonly used in radiographic examination of the pregnant woman's abdomen or pelvis may add to the small chance that her child would develop leukaemia during the early years of its life. The Medical Research Council examined this view extensively, for the histories of 40,000 mothers who had been irradiated during pregnancy were collected and information obtained about the children born to them; the incidence of leukaemia was not increased.

There are now "Home Office Requirements for the Control of Shoe-fitting Fluoroscopes". It seems rather regrettable that the Home Office should have to bother at all to shield the public from retailers who have no conception of the potential dangers of X-rays. Far better to abolish their use in shops.

When the next Report of the Scottish Committee, under Lord ADRIAN, appears readers will then have 4 invaluable books of reference on the present radiation dangers to the populations of the world. *S. Russ*

MINISTRY OF HEALTH: DEPT. OF HEALTH FOR SCOTLAND. **Radiological Hazards to Patients. Second Report of the Committee** [ADRIAN (Chairman)]. 114 pp., 9 figs. (2 on 2 pls.) 1960. London: H. M. Stationery Office. [6s.]

The considerations that gave rise to this enquiry are those concerning the long-term genetic hazard to the population as a whole, arising from the average radiation dose received by the population in excess of that from natural sources. It may at once be said that this excess is contributed in the main by diagnostic radiology.

The Hazards to Man of Nuclear and Allied Radiations was compiled by the Medical Research Council in 1956 [see this *Bulletin*, 1956, v. 31, 1054]. Reference to this valuable Report is often made in the present text and in particular to the different levels of safety in radiation to the population recommended in the two Reports. The Report of the Medical Research Council though wide in scope was restricted in one important respect in that enquiries were conducted among only 5 different hospitals. The present Report, though not so wide in scope, is the result of an enquiry of an elaborate character among 376 hospitals chosen in England, Wales and Scotland. Two questionnaires were circulated, one for a week beginning in April, the other for a week in December 1957.

There was a good response to the request for information; for the week beginning in December returns were made by 343 out of 376 (91%). Some idea of the work involved in this survey will be gained by considering the

numbers involved. During the week of the first survey the total number of radiological examinations carried out in National Health Service hospitals and chest clinics was 259,447. For the second survey the corrected total was 220,260.

The annual genetic dose from general diagnostic radiology in the hospitals amounts to 13·2 mr, to which a small increment estimated at 0·9 mr has been added to take into account general diagnostic radiology performed outside the National Health Service. This total of 14·1 r is appreciably less than the 22 mr per head per year shown by the Medical Research Council Report 1956. This is all to the good; moreover in the Report the view is expressed that even this small dose can be reduced by scrupulous attention to clinical and technical possibilities. In section 166 of the Conclusions (p. 45) we read:—"If the recommendations which we have set out below are carried out we are satisfied that the total annual genetic dose to the population from all forms of medical radiology can be reduced to a figure of 6 mr. or less".

From time to time someone challenges the warrant for carrying out mass radiography. There is an excellent reply to any such challenge; data for 1958 show that just over 4¼ million mass radiography examinations were made in Great Britain. They led to the discovery of 17,569 cases of pulmonary tuberculosis requiring supervision, 3,503 cases of lung cancer, 10,161 cardiac abnormalities and 3,741 cases of pneumoconiosis. The enquiry showed that such examinations are a relatively unimportant source of gonad radiation exposure.

The Report is a model of its kind; it is packed with vital information and readers may look forward to a Report which will deal with somatic effects. *S. Russ*

WATSON, Bernard B. [Edited by.] **The Delayed Effects of Whole-Body Radiation: a Symposium jointly sponsored by the Operations Research Office and the Walter Reed Army Institute of Research.** pp. ix + 80, 4 figs. 1960. Baltimore 18: Johns Hopkins University Press, Md., U.S.A. (for Operations Res. Office). London: Oxford University Press, Amen House, Warwick Square, E.C.4. [36s.]

These 7 symposium papers with the lively discussions they evoked may be expected to provide a "useful summary of the current state of knowledge about the delayed effects of whole-body radiation". There is not, in the text, a strict adherence to whole-body irradiation, for experiments are cited in which only parts of the body are irradiated but they still have a relevance here.

The subject-matter falls into 4 groups:—Life-span Effects, Malignancies, Cataracts and Genetic Effects. The symposium starts with a mathematical paper by G. A. SACHER, pp. 3–10, and the author expresses his outlook in the following terms:—"My view is that the path to interspecies prediction of lifetime effects is through the development of a quantitative theory of mortality and ageing". In the discussion (pp. 14–16) exception was taken to the assumption that ageing is a unitary process. N. I. BERLIN (pp. 11–13) dealt with the effects of chronic ionizing radiation on the life-span of man. He admitted that there were no data available for man; the enquiry into a possible shortening of the life-span of radiologists compared with that of other physicians led to no definite conclusion. Reference is made to the preceding mathematical paper but Bertin considers that the extrapolations cannot and should not serve as a basis for estimating the hazard to man involved in exposure to ionizing radiation. Malignancy can be produced in man and the lower animals by radiation.

IRENE U. BOONE (pp. 19–38) gives a long account of the latter, the animal used for experiment being the mouse. The commonest malignant conditions in the mouse are leukaemias, endocrine, mammary and lung tumours. Leukaemias occur rather frequently in the mouse and this can be increased by irradiation; the induction occurs with a shorter latent period than that shown by the controls. L. H. HEMPELMANN (pp. 38–47) reported on malignant disease in population groups exposed to radiation. 5 groups were discussed:—children exposed to partial body radiation, patients (British) with ankylosing spondylitis treated with X-rays to the spine, Japanese survivors of atomic bombing, American radiologists and children exposed to radiation prenatally.

D. V. L. BROWN (pp. 51–58) gave an account of radiation cataracts in animals. He thought it was now generally agreed that, in early stages, radiation results in a characteristic clinical picture that differs from all other types of cataract. The effect of the rays is a direct one upon the lens structures and is not due to a blood-borne poison, as others have postulated. The lens being an encapsulated organ there is no exit for damaged cells and as they accumulate so sight becomes impaired.

D. G. COGAN spoke on *Radiation Cataracts in Man* (pp. 59–65). From his own observations he concluded that the threshold dose for radiation cataracts produced by 100–200 KV X-rays was of the order 600 r.

D. GRAHN (pp. 73–80) wound up with a highly interesting account of genetic alterations in animals and man. Strange to relate it brought forth no discussion.

Not the least valuable part of this publication is the bibliography to be found with every subject discussed. *S. Russ*

LEE, W. R. & APPLETON, G. J. **A Defective Radioactive Source in Industry.** *Ann. Occup. Hyg.* London. 1960, Nov., v. 2, No. 4, 274–7, 1 fig. on pl.

Systematic tests of personnel exposure to radiation bring their reward. In the present instance no harm resulted to the operator. The monitoring film badge when not worn was put in a drawer near to contaminated equipment. The source was a sealed Cobalt unit the gamma rays from which were used in radiographic tests upon boilers [this *Bulletin*, 1957, v. 32, 976]. The average fortnightly dose recorded per individual was less than 100 mr. On the occasion of this particular test the lapel film gave a dose assessment of 1470 mr. and the wrist film 2130 mr. Over the same period the man's quartz fibre electrometer recorded only 20 mr. It was clear that the over-exposure of the film took place in non-working time and a search disclosed a leak in the container.

The paper concludes with brief descriptions of four methods of detecting any such leaks that may occur as a result of some not necessarily gross damage to the radioactive container. *S. Russ*

WORLD HEALTH ORGANISATION. TECHNICAL REPORT SER. No. 196. **Medical Supervision in Radiation Work. Second Report of the Expert Committee on Radiation. Geneva, 28 September–3 October 1959.** 31 pp. 1960. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr.1.–.]

This Report is the result of a meeting of experts in Geneva held from September 28th to October 3rd, 1959. There may be a little surprise at the long delay in publication of a brochure of 31 pages. The hope is expressed that the results of this meeting will be of considerable help and provide valuable guidance to medical and health personnel engaged in establishing health protection programmes. The chief duties of the medical officers responsible for the medical aspects of the health programme, include the selection of radiation workers, the continuing evaluation of work assignments and the diagnosis and treatment of radiation injury.

In general it is impossible to associate specific exposure risks with particular industries or group activities and it is necessary for the physician to determine the hazards to which people under his supervision are potentially exposed. The major categories of radiation work and their associated risks are discussed in the course of this Report.

It is becoming yearly more obvious, with the growth of radiation work the world over, that the medical people involved will have to possess a considerable knowledge right outside any medical curriculum and just as the academic diplomas in radiology arose from the need of systematic instruction in radio-diagnosis and radiotherapy, so in the near future some new qualification for radiation medical officers may well arise. This is not in the text of the Report, but the reader may feel that the comprehensive knowledge foreshadowed in this Report as indispensable for the carrying out of his protective duties can only be got by systematic instruction over quite a period.

S. Russ

KLAUDER, J. V. **Patch Test Study to determine Cutaneous Reaction to New Compounds.** *Arch. Environment. Health.* Chicago. 1960, Nov., v. 1, No. 5, 407–16, 4 figs.

The practical usefulness of the several methods of patch testing in showing whether a substance has a primary irritant or an allergenic action is illustrated in groups of 50 subjects, fewer than generally recommended. In prophetic patch tests, the first application remains on the skin for 2–5 days, the second, 2 weeks later, for 24 hours. In repeated insult patch tests the substance remains on the skin for 24 hours on alternate days for 10–15 applications, and 2 weeks later the challenging application is made and sometimes retesting is done 2 weeks afterwards. Open tests simulate usage. Patch tests combined with usage are ideal when practicable.

The reactions observed in this study are essentially allergic reactions and fatiguing reactions—the former resulting from an alteration in the subject caused by previous exposure, the latter from repeated exposure to substances which are inherently irritant in some concentration or degree of exposure, *i.e.*, an accumulative irritant. A primary irritant is an irritant in that concentration which on first contact causes inflammation. Inflammation may vary in degree. A strong irritant causes reaction in everyone, a weak irritant in some, and as the concentration is increased the incidence of reactions increases. Unlike the allergic reaction, the fatigue reaction may not reappear with a lower concentration, if the application site is changed, or on challenge or retesting. The fatigue reaction may appear early or late, the allergic reaction after a minimum of a week after the first sensitizing exposure. In prophetic testing, reaction after the first application indicates primary irritant action or else incidental sensitization.

On repeated insult tests, 3·3% triethylenediamine caused immediate irritation in 2 subjects, who remained negative when the concentration was reduced, and later, as predicted, some of the other 50 who had been negative showed fatigue reaction but not on changed sites, and challenge was negative in all: the dermatitis potential would be above 3·3% in use. A silicone solution produced fatigue reaction in 25 and 2 showed reaction on challenge but not on retesting, the last excluding allergy. An organic phosphate insecticide, in pilot tests with 10% solution was irritant; 5%, the proposed strength for use, was negative until after 10 applications when many had become allergic: it should not be used if it entails skin exposure. An epoxy resin, negative at first later produced severe allergic reactions. It was a potent sensitizer undesirable for further study.

M. Patricia Fitzsimons

CHANTRAINE, R. Dermatoses professionnelles des mineurs **[Industrial Dermatitis in Miners]** *Rev. Inst. Hyg. des Mines.* Hasselt. 1960, v. 15, No. 2, 41–5. [10 refs.]

This is a general account of the aetiology, diagnosis and prevention of industrial dermatitis as it occurs among workmen at Belgian coal-mines. It is based on experience of cases investigated at the department of dermatology of the University of Liège. The interest of the contribution is that it reveals that the problems of dermatitis among Belgian coal-miners are similar to those in Great Britain; thus mycotic infections are common and their prevalence is attributed to the use of pithead baths.

A. Meiklejohn

KLEINE-NATROP, H. E. Berufsbedingte Paladonekzeme bei Zahntechnikern. **[Occupational Eczemas caused by Paladon in Dental Mechanics]** *Berufsdermatosen.* Aulendorf. 1960, Dec., v. 8, No. 6, 301–5.

In this paper there is an account of the manufacture of Paladon—a polymerized methylmethacrylate—used in making dentures. Eczemas are well known to occur in those who handle the chemicals used in the process. There are difficulties in ascertaining the particular substance or substances which may result in allergic manifestations because there are different methods of

manufacture and manufacturers are not very communicative about the processes they use. Some description is given of the stages in the synthesis of Paladon and of the additives employed as catalysts, accelerators, inhibitors, stabilizers and plasticizers.

In conclusion it is stated that the liquid monomer methylmethacrylate is primarily the allergen but that occasionally the additives may act in this way. It is also to be expected that at the present time with the more frequent use of self-hardening plastics there will be an increase in the number of Paladon eczemas among dentists, dental mechanics and others.

M. E. Delafield

WEBER, G. & BARNISKE, R. Paraform-Hyperkeratosen nach Art des Keratoma palmare et plantare. [**Paraform-Hyperkeratoses of the Keratoma Palmare and Plantare Type**] *Berufsdermatosen.* Aulendorf. 1960, Dec., v. 8, No. 6, 306–12, 4 figs. [18 refs.]

Paraform, a mixture of high polymers of formaldehyde, is used in the manufacture of artificial rubber and plastics. It is known to give rise in some workers to dermatitis and eczema but the literature appears not to contain any reports on hyperkeratosis resulting from contact with the chemical although it is known to be split up into formaldehyde in the presence of moisture.

Reported in this paper (with photographs) are 4 cases of palmar hyperkeratosis in paraform workers. In 2 of these there were also similar skin changes in the soles of the feet. There is a discussion of these cases and in particular of the localization of the skin lesions to hands and feet, for in other workers in the same factory there were cases of more generalized eczema of hands, arms and face. The works doctor stated that hyperkeratosis and eczema never appeared together or consecutively in the same worker. *M. E. Delafield*

FANINGER, A. Berufsdermatosen durch Trichome von Cerealien. [**Occupational Diseases caused by Trichomas of Cereals**] *Berufsdermatosen.* Aulendorf. 1960, Dec., v. 8, No. 6, 313–18, 4 figs.

This paper contains an account of dermatoses of papular urticarial type which have been observed in 2 groups of women engaged in work in which their arms and hands came into contact with the trichomes of a variety of cereals. In the first occupation which is described epidermal growths—the trichomes—are separated from the seeds of black millet for use in brush, broom and other manufactures. 48 women in this occupation suffered from the skin condition and were investigated. In the second occupation women in a slaughterhouse cleaned out pig's intestines and hence came into contact with maize, barley and oats on which the animals had been fed. 18 women were affected.

Investigation indicated that the skin condition in both occupations is due mainly to the mechanical irritation of the trichomes of these cereals. There are photographs to show the sharp, hairy outgrowths which constitute the trichomes. In addition to the mechanical factor skin tests with cereal antigens indicated that an allergic factor may also be assumed to be present. *M. E. Delafield*

RUYS, A. C., VAN DER SCHAAF, A., JAARTSVELD, F. H. J. & VAN NOORD, H. Erysipeloïd bij visbewerkers. [**Erysipeloid in Fish Handlers**] *Nederl. Tijdschr. v. Geneesk.* 1960, Nov. 26, v. 104, No. 48, 2388–91. [12 refs.] English summary.

Erysipeloid is described as an occupational disease of fish and meat handlers. The relationship of *Erysipelothrix insidiosa* (characteristics described) to the disease is discussed. The clinical picture of a self-limiting disease, not followed by immunity, is given; penicillin apparently hastens recovery.

In an investigation of the problem in the Netherlands (Ijmuiden, Amsterdam, Zeeland and Ameland) during the period 1955–60, specimens of fins, fish gastro-intestinal contents, fish meal, slime from a whaler, scrapings from boxes, etc., were placed in broth, then plated on to phenylethanol medium. If there was no primary growth, 3–4 weeks of refrigeration, or storage at room temperature, gave a higher yield. Colonies being "rough" were considered unsuitable for serology but haemagglutination suggested possible sub-groups.

Results:—(1) In the tested areas, fish gave a high percentage of positives, especially mackerel (35—in the latter case—out of 41 tested, with 3 doubtful positives). (2) Fish meal and whaler were all negative. (3) Out of 15 blocks in Amsterdam butcheries, 3 were positive.

Some of the strains resembled *E. insidiosa,* others *E. muriseptica.* One non-pathogenic (to mouse or pigeon) mackerel strain, protected pigs against re-infection.

Difficulty was experienced in assessing the pathogenicity of various strains in man. Experimentally a chlorine preparation (0·4% Halamid) for disinfection was successful, but not so in application.

The origin of the organisms is obscure, as fish caught elsewhere were usually free of infection. The incidence was found to be seasonal, being maximal in the summer when large quantities of mackerel are handled.

Kurt Schwarz

HEATING, LIGHTING AND VENTILATION

OPPL, L. & VASÁK, V. **An Indirect Method for Measuring Ventilation Rates.** *Ann. Occup. Hyg.* London. 1960, Nov., v. 2, No. 4, 243–8, 6 figs.

One method of determining the rate at which a room is ventilated is to liberate some tracer gas or vapour into the room, and then to measure the rate at which the concentration of that substance in the atmosphere declines as the result of dilution by the ventilating air. The authors have used carbon monoxide, in non-toxic concentrations, as a tracer gas, and have measured the concentration of CO by means of an infra-red gas analyser. It is desirable that the tracer substance should be of about the same density as air, so as to promote good mixing, and this requirement is fulfilled by CO.

In closed rooms ventilation rates of about $\frac{1}{2}$ to $\frac{3}{4}$ of an air-change an hour were measured. A few examples of the effect of opening windows are given.

Thomas Bedford

See also p. 382, BLOWERS & CREW, **Ventilation of Operating-Theatres.**

See also p. 382, LIDWELL & WILLIAMS, **The Ventilation of Operating-Theatres.**

Food and Nutrition

The order in this section is:—**General; Foodstuffs; Food Poisoning.**

FOODSTUFFS

Composition and Bacteriological Control

ROSENBLUM, I., STEIN, A. A. & EISINGER, G. **Chronic Ingestion by Dogs of Methyl Bromide-Fumigated Food.** *Arch. Environment. Health.* Chicago. 1960, Oct., v. 1, No. 4, 316–23. [12 refs.]

Dog chow fumigated with methyl bromide was fed to growing beagle dogs at levels of 150, 75, and 35 mgm. bromide per kgm. body weight per day. A control group received untreated dog chow, and an additional group received untreated chow plus a daily supplement of 128 mgm. sodium bromide per kgm. The animals who had the highest intake of methyl bromide became obese and lethargic although their food intake was unimpaired. In all other groups intakes and weight gains were normal. No haematological or biochemical abnormalities could be demonstrated throughout the period of investigation which lasted for more than one year, and post-mortem examination at the end of the experiment revealed no significant pathological changes. 3 dogs died during the investigation, but their deaths could not be related to the ingestion of bromide. Although blood bromide levels were elevated in all the dogs who received methyl bromide or sodium bromide, only those with the greatest intake of fumigated chow appeared to be affected by a depression in metabolism. However, despite blood levels of 34–41 Mq per litre, they showed no other signs of bromide intoxication. It was concluded that the amounts of methyl bromide likely to be consumed by human beings in fumigated food were well below one-hundredth of the quantities given to the dogs who showed no adverse effects, and that therefore food fumigated with methyl bromide could be considered safe for human consumption

R. Schwartz

See also p. 336, FEDERATION PROC., **Proceedings of a Symposium on Problems in Toxicology held in Chicago, Illinois, April 13, 1960.**

FOOD POISONING

PHILBROOK, F. R., MACREADY, R. A., VAN ROEKEL, H., ANDERSON, E. S., SMYSER, C. F., Jr., SANEN, F. J. & GROTON, W. M. **Salmonellosis Spread by a Dietary Supplement of Avian Source.** *New England J. of Med.* 1960, Oct. 13, v. 263, No. 15, 713–18. [13 refs.]

104 cases of salmonellosis occurred among the 1,850 persons in a Massachusetts institute for mental diseases in December, 1958.

The causative organism was *Salmonella typhi-murium*; there were 6 deaths, but 2 were only partly attributable to the infection. The cases occurred within 6½ days and mostly among the older and more debilitated patients.

Egg-nog made with fresh eggs, pasteurized milk, vanilla and sugar was strongly suspected as the vehicle of infection. Egg-nog prepared from eggs received from the same flock was involved in 2 previous outbreaks in the same institute and one in another mental-disease institution. 94 of the 5,050 hens in this flock showed antibodies

to *Salm. typhi-murium*; *Salm. typhi-murium* was isolated post mortem from some of the hens giving a positive agglutination test, and also from 3 of 1,117 eggs from these hens. *Salm. typhi-murium* strains from hens, eggs, and patients were phage type 1 var 5 (Central Enteric Reference Laboratory and Bureau, London), whereas 10 randomly selected cultures of *Salm. typhi-murium* from Massachusetts chicks and also human beings, belonged to other types.

Egg-nog is widely used as a dietary supplement in mental institutions and it was thought to have been responsible for other outbreaks during the past 5 years.

It is emphasised that it would be easy to dismiss eggs as a source of infection if a few only were examined, also that the small percentage of eggs contaminated would result in an occasional sharp outbreak only; a relatively small proportion of eggs are used for egg-nog, the remainder being adequately cooked.

It was recommended that egg-nog should always be pasteurized before use. *Betty C. Hobbs*

WINKLE, S., ROHDE, R. & ADAM, W. *Salmonella*-befallene importierte Kokosraspeln als eine weitere gefährliche Infektionsquelle. [**Imported Desiccated Coconut as a New Source of Dangerous Contamination with Salmonellae**]. *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 4, 583–6.

In April and May, 1960, 12 samples of desiccated coconuts from Ceylon were examined in a Hamburg laboratory and yielded Salmonella Java. Like the strains from Java described by KAUFFMANN, that from Ceylon was also monophasic. Of 71 other samples of coconut examined, 10 were positive for salmonellae, which included *Salm. paratyphi B* (1), Salm. Java (2), Salm. Stanley (1), Salm. Chester (1), Salm. Perth (2), Salm. Lethe (1), Salm. Waycross (2).

Stress is laid on the patchy distribution of salmonellae in the samples examined. The authors usually added 50–150 gm. amounts to selenite medium and subcultured at 24 and at 48 hours on to phenol-red-brilliant-green agar and SS-agar.

Virtually all the desiccated coconut imported into West Germany comes from Ceylon, where hygiene in coconut-processing factories is minimal.

Ten days after the isolation of Salm. Waycross from coconut, the authors were sent a blood culture from a woman with a septicaemic illness which proved to be a Waycross infection. In an addendum to the paper, mention is made of 2 Salm. Stanley infections associated with coconut and of further isolations of pathogens, which included Salm. Bareilly, Salm. Newport, Salm. Ferlac and a new serotype of the Arizona group. *B. Moore*

NORTH, W. R., Jr. **Use of Crystal Violet or Brilliant Green Dyes for the Determination of Salmonellae in Dried Food Products.** *J. Bacteriology.* 1960, Dec., v. 80, No. 6, 861.

WHITEHEAD, T. P. & PRIOR, A. P. **Lead Poisoning from Home-Made Wine.** *Lancet.* 1960, Dec. 17, 1343–4, 2 figs.

This is a fascinating account of a case of severe lead poisoning, now a rare condition although occasional cases occur from the ingestion of lead from "bizarre sources" which have included lead nipple shields, batteries burned on domestic fires and even the lead in the print of newspaper used as toilet paper.

The patient, a village butcher aged 52, was admitted to hospital in November 1958 for epigastric pain of 3 weeks' duration. A tentative diagnosis of lead poisoning was made on the evidence of the blood picture and a daily urinary excretion of lead of 0·31 to 0·4 mgm. Discharged over Christmas, he was re-admitted in early January for an epileptic fit. A certain diagnosis of lead poisoning was then possible on the results of investigation by electroencephalogram, the blood picture and urinary excretion of coproporphyrins and up to 1·0 mgm. of lead in 24 hours. Treatment with calcium disodium versenate resulted in the urinary excretion of as much as 17 mgm. of lead on one day and he recovered completely.

During his first stay in hospital the patient was questioned about his work, hobbies and diet. He admitted that he was "an enthusiastic maker and drinker of home-made wine" and had been for 20 years. Investigations of his diet, the well-water of his home and the beer at his "pub" were all negative. His wine-making equipment was inspected but appeared to be in order.

After the second stay in hospital the search for the source of lead was intensified and was successful. The elderberry wine was found to contain 7·5 mgm. of lead per litre. In its manufacture the ripe fruit was first soaked and at a later stage allowed to ferment in an earthenware vessel known as a "jowl". This jowl, inherited from an aunt in 1958, was found to be over 100 years old and a relic of the age when such containers were glazed with soft lead glazes. Tested with a 1% solution of acid, the jowl yielded 1000 mgm. of lead per litre.

The patient had been consuming about 2 pints of the wine a week.

There is a short but interesting discussion and the warning that in the production of home-made wines antique earthenware vessels should be avoided. *M. E. Delafield*

Mycoses and Mycology

The order of diseases and fungi in this section is:—**General; Dermatophytes; Blastomyces; Histoplasma, Sporotrichum, Phialophora; Candida, Cryptococcus; Actinomyces, Nocardia; Aspergillus; Others.**

Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN.

RIETH, H., SCHÖNFELD, J. & SCHIRREN, C. Beziehungen zwischen humanen und animalen Dermatomykosen. 4. Mitteilung. Sollen spontan heilende Mikrosporien bei Katzen und Hunden wie beim Menschen behandelt werden. [**Relationship between Human and Animal Dermatomycoses. 4**] *Bull. Pharmaceut. Res. Inst.* Osaka-Takatsuki. 1960, Sept., No. 28, 1–8, 4 figs. [32 refs.]

In this paper the authors consider the incidence of dermatomycoses in animals, particularly dogs and cats, and discuss the question of the importance of these infections in relation to their spread to man. In a recent survey in the United States it was found that 200 out of 524 cats and 368 of 1,659 dogs were infected. *Microsporum canis* was the most frequent infecting organism in both cats and dogs; *Microsporum gypseum* was much less common and *Microsporum audouini* was an exceptional finding.

The importance of correct diagnosis for guiding therapy is stressed and this can more readily be secured nowadays because of the ever-increasing number of mycological laboratories. The factors and principles to take into account in treatment are described but without specific mention of the medicaments that are available.

Spontaneous healing of the mycotic lesions may occur in both animals and man. This and the finding that many animals though apparently healthy have a mycotic infection are important in the epidemiology of the mycoses.

In summary it is stated that microsporosis in cats and dogs which is easily overlooked may be the origin of sporadic, endemic and epidemic infections in man. The problem is an important one which requires for its solution a close collaboration between the medical and veterinary services to secure adequate treatment of infected animals and man and the prevention of spread.

M. E. Delafield

FRIEDMAN, Lorraine, DERBES, V. J., HODGES, Elizabeth P. & SINSKI, J. T. **The Isolation of Dermatophytes from the Air.** *J. Investigative Dermat.* 1960, July, v. 35, No. 1, 3–5, 3 figs.

This work serves chiefly to emphasize the necessity of making direct microscopical examinations of material from lesions suspected of being caused by dermatophytes, in order to establish a correct diagnosis. Culture alone may be misleading, as the experiment showed.

Petri dishes containing culture medium were exposed to the air of rooms frequented by patients suffering from dermatophytoses, *viz.*, the waiting hall, examining room, and laboratory where the samples were collected. After incubation the culture media which had been exposed yielded colonies of *Trichophyton tonsurans* and *Microsporum audouini*. Colonies of other dermatophytes such as *T. rubrum* and *T. mentagrophytes* were not obtained in this manner.

It was also found, in a survey of 134 children, that 88 of this number yielded positive cultures of *T. tonsurans*; whereas in only 22 was it possible to demonstrate the fungus microscopically in the hair. *C. J. La Touche*

MANY, H., DERBES, V. J. & FRIEDMAN, Lorraine. ***Trichophyton rubrum*: Exposure and Infection within Household Groups.** *Arch. Dermat.* 1960, Aug., v. 82, No. 2, 226–9.

Relatively few authors have published work on the subject of familial spread of infection due to *Trichophyton rubrum* [see this *Bulletin*, 1954, v. 29, 618; 1957, v. 32, 574]. It is therefore interesting that further investigations have been carried out in this field in New Orleans.

These investigations included detailed clinical and mycological examinations of 127 subjects distributed in 30 households. 97 subjects of negro race inhabited 24 households, while 30 subjects of Caucasian race inhabited the remaining 6 households.

"The overall incidence of infection among the sexes was about equal." The age range over which incidence occurred was earlier for men than for women. The duration of infection within the household varied from 1 month to 35 years (average 4·4 years). Multiple infections occurred in about half the households where exposure to infection lasted more than 1 year.

The lesions were widely distributed on the body. Multiple areas of the skin were found in 63% of infected subjects, while among these only 6·9% presented with infection of the nails, and none presented with lesions on the scalp or genitalia.

Altogether, multiple infections occurred in 37% of the households visited. The distribution of lesions on the skin of these patients was as follows: groin, 56%; buttock, 31%; perianal area, 23%; feet, 14%; nails, 7%.

Among 15 conjugal couples multiple infection occurred in only 2 cases (exposure over 1 year).

A very high incidence of infection among certain genetically related groups as against a low incidence between conjugal couples suggests that one or more hereditary factors may be involved.

C. J. La Touche

COSTA, C. A. & COSTA, L. A. Tinha negra palmar em Belém do Pará. [**Tinea negra of the Hand in Belém, Pará, Brazil**] *Rev. Serviço Especial de Saúde Pública.* Rio de Janeiro. 1960, June, v. 11, No. 1, 219–24, 1 fig.

The English summary appended to the paper is as follows:—

"Three autochthonous cases of 'Tinha Negra Palmar' have been found in Belém, State of Pará, which therefore should be included among the states of Brazil where this mycosis is found. Clinical diagnosis was confirmed by the culture in Sabouraud of material collected from the lesion and by the study of the development and macroscopic and microscopic aspects of the fungus.

"There was a predominance of microscopic structure similar to those of the genus *Cladosporium*, although the authors are aware of the variety of structures which the fungus may present, some similar to those of the genus *Aureobasidium* (=*Pallularia*) and *Dematium*, thus making classification difficult. The authors therefore feel that it should be classified as *Cladosporium* sp. until further studies indicate the position it should be given in botanical nomenclature."

BENEDEK, T. **Critical Survey of the Present Stand of the Production of Perfect Stage of Organs of Fructification in Dermatophytes.** *Mycopathologia.* The Hague. 1960, Dec. 15, v. 13, No. 4, 287–301. [18 refs.]

BAUM, G. L. **The Significance of *Candida albicans* in Human Sputum.** *New England J. of Med.* 1960, July 14, v. 263, No. 2, 70–73, 3 figs. [37 refs.]

What this article emphasizes chiefly is the fact, still not clearly realized by many, that species of *Candida* occurring either as commensals or as contaminants in the mouth, may be isolated from sputum specimens in culture subsequently, because they are expectorated from the mouth with the sputum. Positive findings in cultures from sputum are therefore not conclusive evidence of parasitic activity of these organisms in the bronchi or lungs of the patients thus investigated.

Sputum specimens were obtained from 55 patients suffering from a wide range of systemic diseases and also from 34 hospital employees and from 30 healthy medical students.

Results showed that *Candida* species were cultured from 36% of the hospital employees, 20% of the medical students and 55% of the patients.

[While the conclusion of the author that *Candida* in sputum specimens is of little significance cannot be disputed, many would disagree that its presence in bronchial aspirates is likewise of no significance, especially if it were present in quantity, and few would advocate biopsy in the presence of suspected active pulmonary infection.]

C. J. La Touche

SKINNER, C. E. & FLETCHER, D. W. **A Review of the Genus *Candida*.** *Bact. Reviews.* 1960, Dec., v. 24, No. 4, 397–416. [227 refs.]

KASE, Alice & MARSHALL, J. D., Jr. **A Study of *Cryptococcus neoformans* by means of the Fluorescent Antibody Technic.** *Amer. J. Clin. Path.* 1960, July, v. 34, No. 1, 52–6, 2 figs.

The authors demonstrate in this article the specific staining property of fluorescent antibody when used on cells of *Cryptococcus neoformans* in smears on slides, or present in sections of the host tissue.

Rabbit serum was prepared by inoculating rabbits intravenously on 10 consecutive days with 3 ml. of a formolized 4-day-old suspension of *C. neoformans* and then collecting it for storage when its agglutinin titre had reached 1:160.

The fluorescent substance, fluorescein isothiocyanate, was combined with amounts of *C. neoformans* antiserum and with normal rabbit serum by the method described previously by MARSHALL *et al.* (*Proc. Soc. Exper. Biol. & Med.*, 1958, v. 98, 898) and "then dialyzed until free of unconjugated fluorescein, filtered through a millipore HA membrane filter, and stored at 4°C. until used."

This fluorescent antibody serum stained the cells of all strains of *C. neoformans* treated in this manner, except one, irrespective of the amount of capsular substance surrounding them and irrespective of their source of origin. It did not stain the cells of other yeasts such as *Candida* sp., or *Saccharomyces cerevesiae* or other pathogens such as *Histoplasma capsulatum* or *Blastomyces dermatitidis*.

Fixation of the cells of *C. neoformans* by a number of methods in no way affected their staining by fluorescent antibody. This fluorescent staining was exhibited alike by pathogenic and non-pathogenic strains of *C. neoformans*, but these organisms were not stained when the fluorescent substance was applied to them in normal rabbit serum or rabbit serum prepared against other fungi.

It is well known that certain strains of *C. neoformans* produce only a minimum of capsular substance and are accordingly difficult to distinguish from other yeasts or the yeast phase of other fungi when examined in black ink or nigrescin preparations. Staining by means of fluorescent antibody therefore provides the advantage that such strains of *C. neoformans* can be as readily distinguished from other yeast-like organisms as are strains of *C. neoformans* with wide capsules.

C. J. La Touche

CARNECCHIA, B. M. & KURTZKE, J. F. **Fatal Toxic Reaction to Amphotericin B in Cryptococcal Meningo-Encephalitis.** *Ann. Intern. Med.* 1960, Nov., v. 53, No. 5, 1027–36, 6 figs. [10 refs.]

"1. A case is presented of chronic torular meningoencephalitis treated with amphotericin B. The efficacy of amphotericin B in clearing the tissues of cryptococci was demonstrated, but clinical improvement was not seen because of the adhesive arachnoiditis.

"2. Reported toxic effects of amphotericin B were confirmed. Fever, nausea and vomiting occurred and were controlled by antihistamines. Elevated blood urea nitrogen disappeared on cessation of the first course of

the drug and did not recur when it was repeated. Heparin and dilution of the drug beyond that recommended failed to prevent chemical phlebitis. A catheter inserted directly into the femoral vein was necessary to make possible the administration of an adequate dose.

"3. After three days' administration of amphotericin B at 1 mg./Kg./d., which followed one month at the daily dose of 0·5 mg./Kg./d., the patient became acutely ill and died two days later. Autopsy demonstrated acute toxic degeneration of the liver and toxic nephrosis."

ROTH, H. L. & WINKELMANN, R. K. **Histochemical Technic for Macroscopic Study of Fungi.** *J. Investigative Dermat.* 1960, Dec., v. 35, No. 6, 353–9, 7 figs.

DAS-GUPTA, S. N., SHOME, S. K. & MAJUMDAR, S. S. **Medical Mycology in India.** *Mycopathologia.* The Hague. 1960, Dec. 15, v. 13, No. 4, 339–76. [Numerous refs.]

Communicable Diseases

The order in this section is:—**Tuberculosis; Venereal Diseases; General Infective Diseases; Other Communicable Diseases.**

For the bacteriology of these diseases see the section on Bacteriology below. For diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

TUBERCULOSIS

ROYAL SOC. HEALTH J. 1960, Nov.-Dec., v. 80, No. 6, 487–506, 8 figs. [20 refs.] **Pulmonary Tuberculosis—the Last Stages?**

This symposium was opened by V. H. SPRINGETT (Birmingham) whose paper was entitled *Clinical and Statistical Aspects* (pp. 487–490).

The recent rapid decline in mortality rate from tuberculosis in England and Wales has been due to chemotherapy but it should not be forgotten that there had been a substantial decline in the previous 100 years. Rates of decline have been greatest in early age and least in the elderly, especially males.

In order to be effective chemotherapy must include an adequate combination of drugs and continue for at least 18 months if the sputum has been positive. Sputum conversion can be achieved in less than a year in every case where the patient is co-operative and the organisms are sensitive to at least 2 of the 3 main antituberculous drugs. The right place for the sputum-positive patient is hospital until tubercle bacilli disappear from the sputum.

Many of the patients treated at home do not take their drugs regularly. The best home treatment is daily streptomycin with 200–300 mgm. of isoniazid given by the nurse at the time of injection.

If all methods of tuberculosis prevention and control are used, if facilities for diagnosis and treatment are available, if the fall in incidence of the disease in young people continues, Springett believes that with the death of the present generation of persons aged 45 and over (in a proportion of whom the disease will inevitably appear) the end of tuberculosis in the community will be in sight.

A. B. SEMPLE (Liverpool) dealt with the role of the local health authority (pp. 491–494). With the advent of specific chemotherapy the chain of infection began to be broken. Hospital beds are now plentiful and owing to this it has been possible to apply powers of compulsory removal and detention to recalcitrant patients with much benefit to themselves and their families.

The importance of the work of the health visitor in preventing the spread of infection and her value in getting contacts to attend the clinic were emphasized.

The Liverpool mass radiography campaign of 1959 took in 472,667 persons (76·5% of the available population over the age of 15 years). The discovery rates of active tuberculosis and lung cancer were 2·3 and 0·35 per 1,000 respectively. In the 45–49 age-group the tuberculosis rates were 4·52 in males and 1·38 in females and in the group over 60 years 5·55 and 0·88 respectively, for persons needing treatment.

The routine BCG vaccination of schoolchildren aged 13–14 years is in full swing with an acceptance rate of 70–80%. Vaccination of the newborn is also done—but not routinely except in tuberculous families.

T. M. POLLOCK (London) dealt with BCG vaccination (pp. 494–498). Much of his paper was concerned with the result of the vaccination trial of the Medical Research Council which showed that in the first 5 years after entry the incidence of tuberculosis in the vaccinated group was one-sixth of that in the negative unvaccinated group.

The finding of a high incidence in original reactors with hypersensitivity (induration of 15 mm. or more to 3 TU) indicates that such children should be given X-ray examinations regularly after leaving school.

The incidence in natural reactors with low sensitivity was lower than in unvaccinated non-reactors, which suggests that a low degree of tuberculin sensitivity is associated with some protection against tuberculosis. The presence of a large group of natural reactors in a community will detract from the value of BCG vaccination in the community and is an indication for vaccination at an earlier age when fewer children are as yet infected.

E. V. KUENSSBERG (Edinburgh) spoke of the family

doctor and tuberculosis (pp. 498–503). In 1951 there were 122 patients with tuberculosis in his (group) practice, and in 1959 there were 19 (7·64 and 1·01 per 1,000 patients respectively). No patient died from tuberculosis in 1959. The general medical practitioner still has an important duty in supervising patients under treatment or removed from the tuberculosis register and in persuading members of their families to be examined or to accept BCG vaccination. Kuenssberg gave examples of failure in communication between chest physician and family doctor and stressed the need for full information about changing methods of procedure so that family doctors could co-operate fully and efficiently.

In the ensuing discussion speakers from the United States, Argentina and England took part. Some of the matters raised are reflected in the replies. Springett agreed that the time had come to use compulsory powers. He recommended chemoprophylaxis for recent tuberculin converters but not routinely for schoolchildren with strong tuberculin sensitivity.

Semple also thought that medical officers of health should look at the powers for compulsory removal seriously in order to get all dangerous infectors under control. There should be an aggressive search for tuberculosis in the community.

Pollock did not feel that the current BCG vaccination programme impedes tuberculosis control by any other method. Case finding through the tuberculin testing of children could be put into operation at any time below the age of 13 years. *H. G. Calwell*

LARSSON, J. & LINELL, F. **Tuberculosis and Mortality in Sweden.** *Acta Tuberculosea Scandinavica.* 1960, v. 39, No. 3, 231–4.

"Analysis of the autopsies performed during a 3-year period (1957–1959) at a large hospital revealed that about half of the cases of active tuberculosis remained concealed until post mortem examination. It may therefore be concluded that the official number of deaths from tuberculosis is probably far too low."

MOBERG, A. & ORELL, S. R. Aktiv tuberkulos i ett obduktionsmaterial. [**Active Tuberculosis in an Autopsy Material**] *Opuscula Med.* Stockholm. 1960, Dec., v. 5, No. 10, 335–8.

The English summary appended to the paper is as follows:—

"During a period of three and a half years from 1957 autopsies were performed in 4,292 cases at Södersjukhuset, which is in 92% of all lethal cases at the hospital. Active tuberculosis was diagnosed at the autopsy in 0·9%, chiefly in the age groups between 60 and 80 years. In 29 of the 39 cases the tuberculosis had not been diagnosed ante mortem though some patients had died soon after being admitted to the hospital. A closer analysis of the cases indicates that an old 'cured' tuberculosis in elderly people may be activated by some other often less serious disease."

MUTOLO, P. & LA BELLA, G. L'epidemiologia della tuberculosi in Provincia di Reggio Emilia nel dodecennio 1947–1959. [**The Epidemiology of Tuberculosis in the Province of Reggio Emilia in the 12 years 1947–59**] *Lotta c. la Tubercolosi.* 1960, July–Aug., v. 30, Nos. 7/8, 606–29, 11 figs.

Situated in the north watershed of the Apennines, the province has a population of 384,804 and is divided into 45 districts. The working population numbers 179,044, more than half being employed in agriculture. About two-thirds of the area is hilly or mountainous. There are one central and three other tuberculosis dispensaries. Medical practitioners and public are co-operative and all but 4·2% of the cases have been followed up. There were 8,553 new cases, equivalent to 1·8 per 1,000 persons, in the 12 years. Streptomycin and PAS have been available in Italy since 1947, when the annual tuberculosis rate in Reggio Emilia was 3 per 1,000: this had gradually dropped to 1·8 per 1,000 when isoniazid came into use in 1952. Annual morbidity rates were at 1·4 in the following 3 years and 1·2 in the next 3.

Deaths from tuberculosis during 1947–59 amounted to 1,205, equivalent to an average annual death rate of 0·25 per 1,000; the death rate declined sharply in 1948 and again in 1952.

When analysed by age-grouping, the average annual morbidity rate was 0·9 per 1,000 up to 4 years, 2·8 in the 5–9 group, 2 at 10–14, 3·4 at 15–19, 2·9 at 20–24 and 2·5 at 25–29. There was first a sharp drop and then a more gradual decline with the older age-groups until the rate was only 0·4 from age 75 on. Men were more often affected than women. When the cases were grouped by profession or other occupation members of religious orders were found to show by far the highest incidence —5·8 per 1,000—and this is attributed to habits of self-denial and mortification and to contact exposure in the performance of their duties.

The state of the 6,020 patients diagnosed between 1947 and 1953 was found to be as follows by 1959; 84·3% were clinically recovered or quiescent, 1·9% had become chronic, 2·3% were still ill, 5·4% had died of the disease and 1·7% had died of other causes; 4·4% could not be traced. The rate of clinical recovery has increased in the 12 years, but so has the rate of those becoming chronic, many of whom would have died without the new drugs.

Epidemiologically, the trend is approaching endemicity in the plains and is in an earlier stage of transition in the hill and mountain districts. Towards the end of, and immediately following, World War II many patients with tuberculosis had left the plain to live at higher altitudes, where they spread infection among the indigenous inhabitants who had until then been less exposed to the hazard of contracting the disease and had less opportunity of acquiring a degree of resistance from subclinical doses of infection.

The population of the province is now being examined by miniature radiography and submitted to the tuberculin test, and a mass vaccination drive is to follow.

J. Cauchi

RAMBELLI, G. Stato e funzionamento del Consorzio provinciale antitubercolare di Ravenna durante l'anno 1958. [**Annual Report of the Antituberculosis Board of Ravenna Province for the year 1958**] *Lotta c. la Tubercolosi.* 1960, July–Aug., v. 30, Nos. 7/8, 630–37.

The Director of the Board states that the number of cases of tuberculosis diagnosed annually in his 3 dispensaries showed a decline from 1949 to 1955 and an increase more recently. There were 412 new cases in 1957 and 465 in 1958, the population having increased from 313,631 to 319,061. The increase was due entirely to pulmonary cases, which rose from 236 to 310: non-pulmonary cases declined from 176 to 155.

There were 23 deaths from tuberculosis in 1958 (24 in the previous year). The mortality rate per 100,000 inhabitants was 7·2 in 1958, 55 in 1948, 78 in 1938 and 112 in 1930 [which is as far back as Rambelli reports]. The author comments on the economic efficiency of the Board's activities which now cost 50 lire per inhabitant.

[A random checking of figures in the tables suggests a number of inaccuracies.] *J. Cauchi*

MOSOLYGO, D. Der gegenwärtige Stand der Ermittlung von Tuberkulosekranken in Ungarn. [**The State of Ascertainment of Tuberculosis in Hungary**] *Santé Publique.* Bucharest. 1959, v. 2, Nos. 3/4, 353–66, 9 figs.

The goal of eradication will not be reached until there is notification of every case of tuberculosis. Effective notification and the adoption of other methods of tuberculosis control were late in coming in Hungary. For example there is evidence that in the period 1931–1940 only an insignificant fraction of cases were known to the public health authorities.

Progress began to be made in 1938 when a chain of tuberculosis dispensaries was established, and between 1940 and 1957 the ratio of tuberculosis physicians rose from 1:178,000 to 1:37,000. There was also a great increase in the number of tuberculosis nurses. The number of dispensaries rose from 88 in 1940 to 185 in 1957.

By 1958 16 mass miniature radiography units had been provided to which 11 others were about to be added, making a total of 27 (13 stationary and 14 mobile). There are also 19 other X-ray units.

The number of persons attending the dispensaries rose from 634,000 in 1943 to 4½ million in 1954. The number of the population X-rayed rose from 388,000 to 3 million.

The number of cases of active tuberculosis diagnosed in 1945 was 20,000. The peak was reached in 1947 when there were about 62,000 since when there has been a gradual but uneven fall to just under 30,000 in 1957. Between 1953 and 1957 the proportion of persons with early disease rose by 13% and that of patients with late disease fell by 10%.

In 1957 70·2% of the 27,940 new patients with active disease came for examination of their own accord because of symptoms; they represented only 12·7% of the total number examined.

The author emphasizes the value of the "open door" in the tuberculosis dispensary. It is better to X-ray 100 persons unnecessarily than to find a single neglected late case.

In the first half of 1958 40% of those found to have active tuberculosis had come for examination of their own accord and 60% had been sent by their doctors. The discovery rates in these groups were 2% and 6% respectively.

The tuberculosis dispensaries carry out routine examinations on adults (school teachers and others in close contact with children, food handlers, transport workers, etc.), on children under 14 and on contacts.

In 1957 the adult group numbered 43·8% of the total 2,980,217 examined and yielded 36·7% of the 8,345 new cases of active tuberculosis discovered. The most important members of this group were the teachers; not all of these were examined, however, and some outbreaks of tuberculosis occurred in schools.

Children under 14 numbered 18·9% of the total and yielded 10·6% of the new cases, but contacts who were only 7·3% of the total yielded 40·0% of the new cases. Miniature radiography was used in 30·0% of the total and yielded 12·7% of the new cases.

A programme of future development is presented. It is hoped that by the end of 1965 it will be possible to X-ray the whole population every 2 years. Compulsory measures would assist in this. Contact examination should be made every 6 months. *All* teachers must be X-rayed regularly. Schoolchildren should be tuberculin tested and only reactors X-rayed; compulsion should be introduced. Every effort should be made to ensure early diagnosis and to have all persons with tuberculosis or suspected of having it under supervision at a tuberculosis clinic. *H. G. Calwell*

SHAH, J. R., WARAWDEKAR, M. S., MEHTA, R. H. & DESHMUKH, P. A. **Tuberculosis Morbidity in Bombay.** *Indian J. Med. Sci.* 1960, Nov., v. 14, No. 11, 948–53.

This paper reports the results of recent tuberculin and mass radiography surveys in Bombay (population 2,840,000 in 1957). The Mantoux test was used with (at first) 5 TU and (later) 1 TU of PPD. The criterion of a positive reaction was induration of 8 mm. or more.

The first group investigated consisted of 1,120 members of 280 families. The families were well housed in model flats but the income was low. In this group 282 children aged 10–14 years and 357 adults aged 15–70 years were tested with 5 TU. The reactor rates were 31% and 95% respectively. 516 adults and 376 children were X-rayed. The discovery rates of active pulmonary tuberculosis were 3·2% in adults and 0·5% in children (total 2·2%).

The second group consisted of schoolboys aged 5–20 years who came from families in the higher income group. 1,066 boys were tested with 1 TU; the reactor rate was 50%. The rates under 14 and over 14 years were 46% and 65% respectively. There was no case of active tuberculosis.

The third group consisted of destitute girls aged 11–20 years who had been taken into welfare institutions from very bad conditions. 116 girls were tested with 1 TU;

the reactor rate was 68%. 3 of 119 (2·5%) had active tuberculosis.

The last group was of hospital nurses aged 17–27 years mostly from poor homes. The reactor rate to 1 TU was 72% in the 84 tested and X-rayed. There was no case of active (or other) pulmonary tuberculosis.

The results show the variation in tuberculosis morbidity that occurs in different groups of the community in Bombay. The incidence is highest in poor groups (family income rupees 100–150 per month) and lowest in the boys from families with an income of rupees 500–1,000 p.m. Morbidity also increases with age.

H. G. Calwell

THOMPSON, J. R. **Pulmonary Tuberculosis in the Aged.** *Amer. Rev. Respiratory Dis.* 1960, Nov., v. 82, No. 5, 682–6, 3 figs.

This paper analyses the autopsies performed at the Municipal Tuberculosis Sanitorium in Chicago, during the 10-year period 1950–1959. There was a total of 801 patients, of whom 569 were men and 232 were women. In a figure in which patients were grouped according to age and decades, it is shown that there was a preponderance of patients in the 3rd, 4th and 5th decades at the beginning of the period, whereas in the later years the majority of the patients fell into the 5th, 6th, 7th and 8th decades. A further figure dealing with patients over 70 years of age, or over, with evidence of tuberculosis at autopsy shows that the number has steadily risen throughout the decade.

According to the histories given the onset of time between the death of the patient and the onset of the disease was less than 5 years in 58 of the cases. Approximately one-half of the patients had evidence of pulmonary tuberculosis with cavitation. Of the 89 patients in the 8th decade, 15 were found to have pulmonary cancer, 18 extrapulmonary cancer. 53 had benign nephrosclerosis, and 39 chronic reactive hepatitis. It is thought that these additional changes may influence the manner in which the host's ability to handle infection such as tuberculosis occurs. A striking factor was the large number of patients in whom the malignant tumours actually invaded the tuberculous tissue, even when it was walled off, and thus reactivated it.

Most of the present cases of tuberculosis in elderly people were uncovered quite by accident.

F. H. Young

STEWART, C. J., EMBLETON, D. P. F. & VAN ZWANENBERG, D. F. **Comparative Tuberculin-Testing of Human Subjects. A Method of Differentiating the Type of Virulent Mycobacterial Infection.** *Brit. Med. J.* 1961, Jan. 7, 7–13, 3 figs. [33 refs.]

The last-named author has already reported [this *Bulletin*, 1960, v. 35, 1191] that during a period of 6 years he had been able to trace the source of infection of about one-fifth of schoolchildren found to be tuberculin reactors at their first test and one-third of those found to have undergone tuberculin conversion by serial testing.

As it was suspected that much of the infection unaccounted for might be due to milk from tuberculous cattle it was decided to carry out simultaneous tests with bovine and human PPD on the children of the area in order to see if comparison of the incidence and sizes of the resulting reactions would be of value in differentiating the type of infection responsible.

The results of such tests in 8,839 children aged 5–18 years living in 7 districts in eastern England are reported. The districts included a city, 1 purely residential area, 1 purely rural area and 4 mixed rural-urban areas.

The Heaf test was used with bovine PPD (1 mgm./ml.) and human PPD (2 mgm./ml.). Full details are given of the procedure and the reading and measuring of the reactions. [The use of the Heaf gun for quantitative work of this kind breaks new ground.]

Reactor rates to each tuberculin and the sizes of the reactions were analysed by area and age and the results compared with the known incidence of registered cases of tuberculosis and of infected milk supplies.

In 2 districts known to have had infected milk and a high incidence of non-respiratory tuberculosis the rate of reaction to bovine PPD was higher than to human PPD and the reactions were larger. In 2 towns with a known clean milk supply and a low incidence of non-respiratory tuberculosis there were more reactors to human than to bovine PPD, and the reactions were larger to human than to bovine PPD.

"In spite of the deficiencies in the design of this investigation and our lack of knowledge of the technique and materials of comparative tuberculin-testing there is evidence in the childhood population of East Suffolk and Norwich that tuberculin-testing with bovine and human PPD given by the Heaf technique will reveal a pattern of reaction which is related to the incidence of human and bovine mycobacterial infection in the area."

Reactions to both tuberculins were found to become larger and less easily differentiated with increasing age, and it was concluded that comparative testing of this kind is best done in childhood before multiple infections with the same or different mycobacteria have confused the issue.

H. G. Calwell

HALL, Marcia. **Reversion of Positive Tuberculin Reactions.** *Med. Officer.* 1960, Dec. 9, v. 104, No. 24, 351–2.

The question of tuberculin reversion [that is the disappearance of natural tuberculin sensitivity previously demonstrated] was studied in children who had attended the tuberculosis clinic of a London hospital.

The original tests had included the jelly and Mantoux tests with 1 or 10 TU and all were "unequivocally positive". The children were retested with 10 TU of OT (Mantoux).

In 12 months of 1959–60 100 children previously recorded as reactors were retested; 26 showed no reaction and 15 had induration of 6 mm. or less. The period elapsing between the original and the present test in each case is not stated but it is clear that in some it was 12 years.

The radiological changes, contact history and (anti-tuberculous) treatment were compared in the persistent reactors and the reverters. There was an excess of children with gross radiological changes when first seen among

the persistent reactors. Reversion was found even after severe initial infection, but in general (although not invariably) the degree and virulence of the original infection determine the persistence of tuberculin sensitivity.

The presence of a household infector did not appear to affect the reversion rate but the evidence was very incomplete.

The final question asked by the author is whether reverters should be vaccinated with BCG. [It is nowhere stated in this paper that the 100 children concerned had in fact suffered from tuberculosis but 60 of them had received specific chemotherapy, and it is mentioned that 18 others would certainly be treated if seen for the first time now. It is not clear why the retesting stopped at 10 TU, and it must be left to speculation how many more would have reacted to 100 TU. The reviewer has often seen children recorded as reactors to the jelly test fail to react to the Heaf test (say 30 TU) and such children when vaccinated with BCG have never shown an accelerated reaction. There is good reason to doubt the accuracy of the jelly test.] Further study is called for by the author. *H. G. Calwell*

Sikand, B. K., Pamra, S. P. & Mathur, G. P. **Relative Merits of Various Schedules in the Domiciliary Treatment of Pulmonary Tuberculosis.** *Pakistan Med. J.* 1960, Nov., v. 11, No. 11, 12–28. [22 refs.]

The authors investigated the relative efficacy, acceptability and cost of 4 different drug regimes in the domiciliary treatment of pulmonary tuberculosis in New Delhi, India. The trials were started in 1956 and included 2,207 patients with active disease. The 1,234 patients who completed at least 3 months' treatment form the material of the analysis.

The treatment schedules were:

A. Streptomycin ½ to 1 gm. daily with isoniazid 50–200 mgm. daily.
B. Streptomycin twice weekly with isoniazid daily (as above).
C. Isoniazid (as above) and PAS 4–10 gm. daily.
D. Isoniazid alone daily (as above).

Patients were allocated at random to one of the above groups, and it was the intention that treatment should continue till the achievement of sputum conversion, cavity closure with or without complete radiological clearing, or radiological stability for 3 months except in group A where, if by 3–6 months' treatment the disease had not become clinically quiescent, further treatment was to be continued under schedule C. Patients in group D who got worse or continued to be very toxic for over 3 weeks were to be changed to streptomycin and PAS.

Sputum conversion was achieved at 3 months in 80·7% of patients in group A, a rate considerably higher than in the other groups. Schedule D was the least satisfactory (50·3% at 3 months and 70·2% at 9 months). The rate shown in group A at 9 months was the same as at 6 months.

As regards cavity closure schedule A was clearly superior to the others. Radiological improvement in this group at 3 months was almost the same as after 9 months with B and C, and D was the least effective.

When the patients were divided into those who took the drugs regularly and those who did not it was found that 6 months' irregular treatment with schedule A was as effective as 6 months' regular treatment with B and C.

Schedule A was considered to be the best; even if it was slightly more costly this disadvantage was offset by its greater acceptability and efficacy. When injections cannot be easily arranged schedule C is the regime of choice. Schedule D should only be used in default of a better regime. *H. G. Calwell*

Rothstein, E. **The Nineteenth Veterans Administration—Armed Forces Conference on the Chemotherapy of Tuberculosis.** *New England J. of Med.* 1960, Sept. 22, v. 263, No. 12, 589–91.

At this Conference, although the main emphasis was on the evaluation of antituberculous drugs, full attention was paid to non-tuberculous diseases of the bronchi. A co-operative study of 630 patients with bacteriologically proved cavitary disease not previously treated with drugs was reported. Half were treated with isoniazid in conventional doses; the other half in doses up to 900–1,200 mgm. daily; no very significant difference was discovered and the toxic reactions upon the higher dosage were 5% compared to 2% with the lower. Another study on lung specimens from 68 patients treated with conventional isoniazid dosage compared the results with those obtained in 68 resections from patients treated with 600–1,500 mgm. daily; no significant difference was discovered.

4 papers dealt with the additional use of steroid drugs, but no great advantage was reported from their use.

37 patients who were treatment failures with other drugs were treated with cycloserine in relatively high dosage (2 gm. daily). In 5 patients major psychoses developed. The main results were a marked decrease of sputum with lessening or disappearance of infectivity which allowed improvement to the point where they could successfully withstand effective thoracic surgery.

Papers were given showing the value of Amphotericin B in the treatment of pulmonary histoplasmosis.

An interesting study was given from the Veterans Administration in Albany, New York. It was found that if hamsters were injected subcutaneously with bronchial secretions from patients with lung cancer, polypoid bronchial epithelial hyperplasia developed in 60 to 70%. This was not found in any controls injected with secretions from patients without cancer. *F. H. Young*

Lotte, A., Noufflard, H., Debré, R. & Brissaud, H. E. **The Treatment of Primary Tuberculosis in Childhood.** *Pediatrics.* Springfield, Ill. 1960, Oct., v. 26, No. 4, 641–53, 4 figs. [13 refs.]

This paper is a report on the enquiry undertaken in 1953 by the Institut National d'Hygiène, Paris, and aimed at assessing the immediate and late results of prolonged chemoprophylaxis in children with recent primary tuberculosis. The control series consisted of patients whose medical advisers had decided not to give

them chemoprophylaxis. This method, although it does not allow the two groups of cases to be picked at random, is probably fairly satisfactory. Patients were divided into 4 age-groups: (1) under 5 years, (2) 5–9 years, (3) 10–14 years, and (4) 15–24 years of age. 4 types of tuberculosis were recognized. Type 1, latent and primary tuberculosis revealed by conversion of skin tests with no clinical symptoms, and a negative fluoroscopy and chest film read by a specialist; Type 2, mediastinal adenitis, but no clinical symptoms; Type 3, clinical symptoms with a normal chest film; Type 4, presence of both clinical and radiographic abnormal findings. Only patients in whom infection had been diagnosed less than 8 months previously were admitted to the study. Treatment consisted of a daily dose of isoniazid, 20 mgm./kgm. in children under 2 years, and at least 10 mgm./kgm. in children over 2 years, without exceeding a maximum dose of 400 mgm. a day. The daily dose of PAS was 300 mgm./kgm. with a maximum dose of 15 gm. a day. Administration was continuous and prolonged, as a rule for 9 months with a minimum of 6 months' duration.

The paper deals with 1,425 cases in which the follow-up exceeded 18 months. Of these, 895 patients received no treatment. As might be expected the incidence of the various complications varied greatly with the age of the children. For various reasons, analysis was only feasible in groups composed of patent forms of primary tuberculosis types 2, 3 and 4 in children under 15 years of age. This group consisted of 1,061 patients, of whom 564 were treated, and 497 received no chemotherapy. In children under 5 years of age the complications observed in the untreated group were: aggravation 6, fatal meningitis 3, lung involvement 3, against 1 pleurisy in the treated group. In the 5–9-year group there were 31 complications in untreated cases; pleurisies 22, lung involvement 5, extrapulmonary involvement 2; as against 1 lung involvement and 2 pleurisies in the treated group. In the 10–14-year group there were 14 complications in untreated cases, consisting of pleurisies 12, lung involvement 1, and extrapulmonary tuberculosis 1; against a single case of pulmonary tuberculosis in the treated cases. Full details of the various complications in the different age-groups are given.

Isoniazid sensitivity of the strains of bacilli isolated are considered under 3 phases: after 3 months of treatment, within the first 3 months of treatment, and before treatment. After 3 months of treatment 16 strains were isolated, of which 11 were sensitive, 2 were highly resistant, and 3 were weakly resistant. 175 strains were isolated in the first 3 months of treatment, of which 4 were definitely resistant, and 1 slightly resistant. As none of these 5 patients had cultures taken before starting treatment, it is doubtful whether this had any effect on the resistance. 4 strains were also found to show high-grade resistance to isoniazid in patients who had received no treatment. These 4 strains were all isolated in 1957. It is concluded that isoniazid resistance in children treated for primary tuberculosis is exceptionally rare.

The study shows that as there was a decrease of more than 80% in the incidence of complications, the authors consider that routine chemotherapy should be resorted to in clinically manifest primary tuberculosis in children and adolescents. In the case of completely latent primary tuberculosis a definite answer cannot be given as yet.

F. H. Young

KENDIG, E. L., Jr. & BURCH, C. D. **Short-Term Antimicrobial Therapy of Tuberculous Meningitis.** *Amer. Rev. Respiratory Dis.* 1960, Nov., v. 82, No. 5, 672–81.

The Committee on Therapy of the American Trudeau Society has advised that the treatment of tuberculous meningitis should be continued for a minimum of 18 months to 2 years [this *Bulletin*, 1955, v. 30, 26]. This paper reports on 19 surviving patients who received antimicrobial treatment for 12 months or less, and on 11 who received the treatment for 8 months or less.

The therapy consisted of isoniazid varying from 6 to 20 mgm. per kgm. of body weight; streptomycin from 40 to 80 mgm. per kgm. of body weight; and PAS 200 mgm. per kgm. of body weight. Streptomycin was discontinued as soon after completion of a 3-month course as activity of the disease permitted. Only 6 patients received intrathecal streptomycin therapy. Corticosteroids were added to the therapeutic regime in 16 cases. The average duration of follow-up was 52 months, with no instances of relapse.

The results were considered good in 16 patients; of the other 3, 2 survived with diplegia and some mental retardation. The other was semi-comatose and had a history of illness of 30 days' duration, and has never completely regained consciousness. It is suggested that, at any rate in selected cases, 12 months' therapy is probably sufficient.

[For an earlier study see this *Bulletin*, 1958, v. 33, 837.]

F. H. Young

See also p. 330, MORROW, **The Results of Chemotherapy in Silicotuberculosis.**

See also p. 326, GERNEZ-RIEUX, BALGAIRIES, VOISIN & FOURNIER, **Pneumoconio-Tuberculosis. Results of Medical and Combined Medical-Surgical Therapy.**

THOMAS, D. E. & ARONSTAM, E. M. **Manpower Salvage with Surgery in Pulmonary Tuberculosis.** *J. Amer. Med. Ass.* 1960, Sept. 3, v. 174, No. 1, 23–5.

During the past few years it has become obvious that the system by which all military personnel who developed tuberculosis were discharged was very wasteful. This paper reports on 432 patients who were submitted to resectional surgery. The report confines itself to those patients in whom it was expected that if everything went well they would be fit to return to duty. 391 patients, of whom 309 were military personnel, were followed up. There was a mortality of less than 1% during the first 30 post-operative days: a cure rate of 97% and a work rehabilitation rate of 98%. Only 4 patients had recurrences of the disease. Of 378 patients in whom complete inactivation of the disease was achieved, 370 were capable of employment; and of these, 131 were returned to active duty. This represents a percentage of 42 out of the military personnel who were followed up.

Patients were operated on from 1953 to 1957, and by better selection for treatment the percentage fit to return to active duty was steadily increasing. As a large proportion of the patients were highly trained officers, or non-commissioned officers, the saving of man-power by resectional surgery is very impressive. *F. H. Young*

STRANDGAARD, E. **On the Significance of Isoniazid Resistant Tubercle Bacilli in Patients with Pulmonary Tuberculosis.** *Acta Tuberculosea Scandinavica.* 1960, v. 39, No. 3, 165–71. [27 refs.]

The author sets out to examine 690 patients treated with isoniazid for at least a month between April 1952 and May 1959. In general the dosage was 100 mgm. 3 times a day. Of these, 65 patients were found to have tubercle bacilli resistant to isoniazid: 31 were resistant to 50 μgm., 2 to 8 μgm., 14 to 1·28 μgm. and 18 with faint or varying resistance; 48 of these patients had cavitated lesions, and 39 were in stage 3. When patients whose treatment had been incorrect were eliminated, 15 patients developed resistant bacilli during treatment with isoniazid and PAS of a correct dosage, but of these no less than 12 had various psychological abnormalities, and there was little doubt that they had cheated and not taken the prescribed PAS. Among patients treated with isoniazid and PAS and in addition 1 gm. of streptomycin every 3 days, 8 patients developed resistant organisms; presumably they had not been taking their PAS regularly, and the streptomycin once every 3 days was insufficient as a cover for the isoniazid.

Since October 1958 urine control with Ehrlich's reagent has been introduced, and not a single case of isoniazid resistance has developed during treatment at the sanatorium.

Finally, isoniazid-resistant bacilli were demonstrated in 3 patients who had apparently not received isoniazid. One was a young male Hungarian refugee with a small fresh lesion; he may be assumed to have become infected in a refugee camp by a tuberculous fellow refugee with isoniazid resistant bacilli. The other 2 were thought to have procured isoniazid to take at home although they denied so doing.

Of the 65 patients, 22 were dead at the end of the investigation, 22 were still affected, and 21 had apparently inactive disease. The prognosis appeared to be most unfavourable with patients with slight or varying resistance, and somewhat better with patients with highly resistant bacilli. As might be expected the prognosis was much worse when the patients had advanced disease, and the patients who had bacilli additionally resistant to PAS fared very badly. *F. H. Young*

LOLLINI, Clelia. Esperienze di vaccinazione con il B.C.G. in Tripolitania. Considerazioni sull'indice tubercolinico e sull'allergia postvaccinale. **[Experience with B.C.G. Vaccination in Tripolitania; Observations on the Tubercular Index and on Post Vaccinal Allergy]** *Lotta c. la Tubercolosi.* 1960, July–Aug., v. 30, Nos. 7/8, 580–96. [Numerous refs.]

A census in 1954 showed an aggregate population of just over 1,091,000 in the 3 regions of Libya—Tripolitania, Cyrenaica and Fezzan—and 315,824 persons (29%) were tuberculin-tested in the 3 years 1953–55, at ages varying from infancy to 21 years. Only 232,436 (73%) returned for the reaction result to be read and 129,297 (56%) proved tuberculin-negative and were given BCG. In Tripolitania and Fezzan during 1956–57 the tuberculin test was carried out on 14,519 schoolchildren and policemen, with a follow-up of 11,712 and BCG vaccination, or revaccination, of 4,474 (38%). During 1957 the test was carried out on 38,576 schoolchildren and other inhabitants of Cyrenaica, 29,800 returned for the result to be read and 12,564 (42%) were vaccinated or revaccinated with BCG.

The author was in charge of the tuberculosis dispensary in Tripoli when WHO and UNICEF launched their BCG campaign in 1953; in 1958 she became BCG team leader under the Libyan Ministry of Health. She now reports her findings in 28,247 persons aged 6 months to 21 years: the tuberculin test was negative in 11,159 and these were given BCG. She discusses the local reactions, which the BCG produced within 3–4 days, and the Mantoux conversion, which showed fading within 2 years. She found the tuberculin index to be high in Tripolitania, higher in men than in women, and considers that the disease has reached the stage of transition from the epidemic to the endemic phase. Rather than undertaking indiscriminate mass campaigns, she advises programmes to be undertaken in well-defined localities and groups. *J. Cauchi*

TENRET, J. **B.C.G. Vaccination in Ruanda-Urundi.** *J. Trop. Pediatrics.* London. 1960, Dec., v. 6, No. 3, 92–7.

The Belgian trusteeship territory of Ruanda-Urundi [which was the north-western part of German East Africa] has an area of 54,172 sq. km. and a population of almost 4,700,000 Africans. The population density is 86 per sq. km., distributed very unevenly.

The country is economically underdeveloped. The average diet is deficient in fats and vitamins A and C; there is sufficient protein but it is almost entirely of vegetable origin. There are probably about 80,000 cases of tuberculosis of which 81% are curable.

A study of the efficacy of BCG vaccination in these conditions was begun in 1955, and at the end of 1959 the results were assessed and conclusions drawn.

Groups composed of the whole population in 3 areas were selected, and the incidence of tuberculosis in them was discovered by mass radiography and tuberculin surveys. Division was then made into 2 sub-groups A and B, identical as to race, nutrition and standard of living. In group A all non-reactors were vaccinated with 0·2 mgm. of lyophilized vaccine while in group B non-reactors were left unvaccinated. No treatment was given in either group.

In group A annual revaccination of the original non-reactors was done, and at the same time new arrivals in the group (by birth or immigration) were tested and if non-reactors vaccinated and subsequently revaccinated with the original group.

The results in 1955 and 1956 before vaccination were compared with those in 1958 and 1959 after the vaccination of non-reactors in group A:

Before BCG Campaign

Groups	No. examined	No. with tuberculosis	Incidence per 1,000	Reactor rate %
A	54,966	665	12·1	50·35
B	28,453	342	12·02	55·34
A and B	83,419	1,007	12·07	52·32
After BCG Campaign				
A	57,348	230	4·01	
B	31,414	360	11·46	

It was found that the appearance of tuberculosis was almost 25 times more frequent where non-reactors remained unvaccinated. It was also found that the protection afforded by BCG vaccination was 7·5 times more effective than that furnished by natural primary infection. The protective action of BCG was more evident at those ages when natural primary infection could be efficiently replaced by BCG vaccination.

The authorities concerned, encouraged by the above results, propose to undertake mass BCG vaccination without preliminary tuberculin testing. *H. G. Calwell*

VENEREAL DISEASES

PUB. HEALTH REP. Wash. 1960, Nov., v. 75, No. 11, 1000–1006. **The Venereal Disease Contact Interview. A summary of papers presented at the Venereal Disease Seminar in Baltimore, April 29, 1959.**

This somewhat discursive article sets out in great detail the methods employed at the John Mahoney Training Center for Nurses, Brooklyn, N.Y., to obtain accurate contact information. The curriculum consists of 2-week refresher courses each month from September to June on epidemiological principles and contact interviewing.

The main part of the article is devoted to the "indirect interview"; by "indirect" is meant obtaining the confidence of the patient before trying to find the contact: in other words, have a friendly chat with the patient before asking for the source of the infection of the patient and the names of those whom he may have infected. Other headings are "The Expander Question", "Education of the Patient" and "Obtaining Contact Information".

The interview may occupy 30–45 minutes and various methods of approach are described; the main objective is to get the patient to talk rather than to talk to him, and only to ask leading questions at the end of the interview after having obtained the patient's confidence. In other words the interviewer should study the pyschology of the patient rather than treat him as a witness in a court of law being examined or cross-examined.

[There is nothing very new here.] *T. E. Osmond*

CARPENTER, C. M., MILLER, J. N. & BOAK, Ruth A. **A "Triple-Test Plan" for the Serologic Diagnosis of Syphilis—a Modern-Day Approach.** *New England J. of Med.* 1960, Nov. 17, v. 263, No. 20, 1016–18, 1 fig. [14 refs.]

The number of serum tests for syphilis, their variety and complexity frequently baffle the average physician.

These authors recommend a combination of 3 tests which should give the necessary answer when the diagnosis is uncertain; these are the VDRL slide test, the Reiter protein complement fixation test (RPCF) and the *Treponema pallidum* immobilization test (TPI). The serum should first be subjected to the VDRL test; if this is negative the patient, with no history or signs of syphilis, may be considered free from syphilis [many will disagree with this; in very early primary syphilis any test may well be negative]. If the VDRL test is reactive or weakly reactive the RPCF test is employed; if this latter is negative the TPI test should be done; if on the other hand the RPCF is reactive or weakly reactive and the VDRL gives the same result the patient is considered syphilitic [here again, surely no one would diagnose syphilis merely on the strength of weakly reactive results with *any* two serum tests for syphilis]. A reactive or weakly reactive TPI test indicates past or present infection with syphilis [many people regard a weakly reactive test as "doubtful" and would not diagnose syphilis on that evidence alone]. A non-reactive TPI combined with a reactive or weakly reactive VDRL test confirms that the VDRL result is a biologically false positive one.

[The combination of the 3 tests recommended has much in its favour but whatever the results they are not 100% reliable.] *T. E. Osmond*

PORTNOY, J. & GARSON, W. **New and Improved Antigen Suspension for Rapid Reagin Tests for Syphilis.** *Pub. Health Rep.* Wash. 1960, Nov., v. 75, No. 11, 985–8.

The stability of VDRL antigens used in the rapid reagin test [this *Bulletin*, 1960, v. 35, 461] for syphilis varies a good deal. In order to obviate this these authors tested the effect of various cations and peroxide on the stability of antigens; results are set out in table 1. They concluded that ethylene dinitrilo tetra-acetic acid disodium salt (EDTA) in a concentration as low as $1{\cdot}25 \times 10^{-4}$ M inhibited deteriorative changes for as long as 3 weeks.

VDRL slide antigen emulsions were prepared (1) in the "usual" way and (2) in a solution of 0·1 M EDTA in distilled water 2·5 ml.; 40% choline chloride in distilled water, 5 ml.; 0·02 M phosphate buffer, 0·2% merthiolate [thiomersal] 10 ml.; and distilled water 2·5 ml.

These 2 antigens were stored at refrigerator, room and incubator (35°C.) temperatures; comparative tests on unheated syphilitic plasma and serum with these 2 antigens

showed that whereas the old antigen varied a great deal in stability the new (improved) one remained stable for 8–25 weeks at room temperature, for 22 weeks or more at incubator temperature and indefinitely at refrigerator temperature; moreover, test results were only very slightly weaker with the new than with the old antigen.

T. E. Osmond

MILLER, J. L., MEYER, P. G., PARROTT, N. A. & HILL, Justina H. **A study of the Biologic Falsely Positive Reactions for Syphilis in Children.** *J. Pediatrics.* St. Louis. 1960, Oct., v. 57, No. 4, 548–52.

This study is based on 400 children; the mothers of these fell into 4 categories—(1) 305 had been treated for syphilis, (2) 73 were biologically false positive reactors (BFP), (3) 18 were STS and TPI negative and (4) 4 had active syphilis. In group (1) 25 children were BFP, 280 normal and none syphilitic; in group (2) 13 were BFP, 60 normal and none syphilitic; in group (3) 7 were BFP, 11 normal and none syphilitc; in group (4) all were syphilitic. Female BFP reactors usually exceed male reactors in the proportion of 71 to 29 [this *Bulletin*, 1957, v. 32, 1044] but in this series of children the respective figures were 55 and 45. No infant born of a treated syphilitic mother had congenital syphilis; of 221 children born of treated mothers 66% showed passive transfer of antibody; of 145 who showed passive transfer 6·9% developed BFP reactions; of 73 children born of mothers with BFP 13 (17·8%) developed a similar reaction. Of the serum tests which gave BFP reactions the Mazzini was most liable to do so, followed by Kolmer and VDRL.

It is stated that 40% of positive serum tests for syphilis in adults are BFP [this statement will make many doctors open their eyes]; it is known that a BFP often presages serious disease and these authors found that 10% of BFP reactors under 18 had systemic disease. In summary 11% of these children gave BFP reactions; 18% of children born of mothers with BFP reactions gave a similar reaction but only 8% of those born of syphilitic mothers did so. *T. E. Osmond*

FIUMARA, N. J. **Treponemal Tests in Diagnosis of Syphilis and Biologic False Positive Reactors.** *Pub. Health Rep.* Wash. 1960, Nov., v. 75, No. 11, 1011–19, 5 figs. [10 refs.]

There are 3 indications for treponemal tests: (1) to distinguish between true and false positive reactions; (2) to establish a diagnosis in patients with clinical evidence of syphilis but negative serum reactions; (3) to aid the diagnosis of syphilis in those who are clinically and serologically negative. In problem cases with persistently positive Hinton tests (or presumably other classical tests with lipoid antigen) the Reiter protein complement-fixation test (RPCF) was used as a screening test; if this was positive a diagnosis of syphilis was made, if negative a TPI test was done.

In general, reagin tests are the most sensitive in primary and secondary syphilis, reagin and TPI most sensitive in early latent syphilis and TPI most sensitive in late cases.

Details of 703 problem patients analysed are set out in detail in tables as regards private or hospital patients, race, sex and marital status; 548 (78%) were found to be syphilitic and 155 (22%) were biologically false positive reactors (BFP).

An interesting fact which emerged was that except in the 15–19 age-group the infection rate increased with age up to 45 years; the BFP rate showed a sharp increase in the 15–19 group.

Of the BFP reactions only 1 showed a reaction higher than 1 in 8 dilution with the Hinton test.

[Many will wonder whether a combination of positive Hinton and RPCF reactions is sufficient to guarantee syphilis in the absence of any other evidence of the disease.] *T. E. Osmond*

DE BRUIJN, J. H. **A Simplified Method for the Preparation of Reiter Protein Antigen.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1960, v. 26, No. 3, 317–20. [10 refs.]

This method consisted of submitting a suspension of Reiter spirochaetes to ultra-sonic disintegration for 10 minutes and centrifuging; to 20 ml. of the lysate are added 60 ml. of saturated ammonium sulphate (*p*H 7·4) with stirring. The whole is refrigerated for 1 hour, centrifuged, the supernatant discarded and the precipitate dissolved in 10 ml. of 0·1 M glycine-saline buffer (*p*H 7·4). The turbid solution is dialysed against fresh solvent until no ammonium sulphate is left. The dialysed solution is centrifuged for 30 minutes at 4,000 r.p.m. and the supernatant employed as antigen; this is freeze-dried after the addition of 0·5% gelatine which appears to have a stabilizing effect. For use the antigen is heated at 37°C. for a few minutes.

When the antigen was compared with a standard product [this *Bulletin*, 1958, v. 33, 33] on a syphilitic human serum results were closely parallel (as shown in a table) but the new antigen appeared more concentrated.

T. E. Osmond

BODENBENDER, R. H. **Shipboard Treatment of Venereal Diseases.** *U.S. Armed Forces Med. J.* 1960, Nov., v. 11, No. 11, 1311–18.

After giving the views of several authors as to the effectiveness of penicillin in the treatment of gonorrhoea this author reports his own experience in treating 83 patients while at sea in the Far East where reinfection could be completely eliminated.

The doses of procaine penicillin employed varied from 900,000 units over 3 days to 3 mega units over 5 days or 4·5 mega units over 3 days; relapses were treated with more penicillin, oxytetracycline or chloramphenicol.

In 68 patients with acute gonorrhoea there was a relapse rate of 14% with the highest dosage, of 100% with the lowest and of 39·7% overall; relapse usually occurred about 14 days after completion of treatment. One long and complicated and one short case report are given.

The author recommends 1·5 mega units of procaine

penicillin G daily for at least 5 days as the treatment of choice of acute gonorrhoea in the male; for relapse oxytetracycline with chloramphenicol in reserve.

[It does seem that the resistance of gonococci to penicillin varies in different parts of the world and this may account for the variability of reports by different authors.] *T. E. Osmond*

GILSON, B. J., TROUT, M. E. & ALLEMAN, H. **Gonococcic Endocarditis.** *U.S. Armed Forces Med. J.* 1960, Nov., v. 11, No. 11, 1375–9.

This case report sets out in great detail the progress of a clear case of gonococcal endocarditis. The patient was a man of 19 who complained of headache, sore throat, and arthralgia involving several joints; there were moderate fever, increased sedimentation rate and tenderness in many areas. There was a history of tonsillitis but not of venereal disease and a family history of rheumatic heart disease. Examination revealed a temperature of 101·2 and pulse rate of 104, sinus tachycardia, a soft systolic murmur but no evidence of gonorrhoeal urethritis; there was a watery discharge in the early stages; various routine laboratory tests including 11 blood cultures were all negative. Finally on the 31st day in hospital gonococci were cultured from the blood.

Early treatment with salicylates had no effect so erythromycin and chloramphenicol were tried; these brought about considerable improvement but when gonococci had been isolated penicillin was employed, first as 2 million units intra-muscularly, and when this was not well tolerated, as a continuous intravenous drip to a total of 732 million units. Recovery commenced and after 2½ months was apparently complete.

T. E. Osmond

SCIPLE, G. W., HOSKING, W. O. & MONTGOMERY, C. H. **A Reappraisal of Benzathine Penicillin in Gonorrhea Control.** *Pub. Health Rep.* Wash. 1960, Nov., v. 75, No. 11, 1007–10, 3 figs.

In order to discover whether "antibiotic quarantine" obtained by the use of long-acting penicillin would reduce the incidence of gonorrhoea these authors employed 4 different treatment schedules: (1) 600,000 units PAM (958 patients), (2) 600,000 units benzathine penicillin (1,075 patients), (3) 900,000 units PAM + 900,000 units benzathine penicillin (1,331 patients), (4) 1,200,000 units procaine penicillin + 1,200,000 units benzathine penicillin (258 patients).

Re-treatment rates after 32 days were highest with schedules (1) and (2) and lowest with the other 2 which were approximately the same. During the period of these trials 1954–59 the morbidity figure rose from 600 to 1,000; there appeared to be no correlation between morbidity figures and type of treatment. When the observation period was extended to 16 weeks re-treatment rates were roughly similar with all 4 schedules. Thus the use of benzathine penicillin appears to present no advantage while it has several disadvantages, *e.g.* extra cost, pain (which may discourage a patient from returning) and possibly the production of resistant strains of gonococci.

T. E. Osmond

MERLE, F. & PEUCH-LESTRADE, R. M. Les équipes semi-mobiles dans la lutte contre la gonococcie au Cameroun. **[Some Mobile teams in the Campaign against Gonorrhoea in the Cameroons]** *Méd. Afrique Noire.* Dakar. 1960, Oct. 1–15, v. 7, No. 19, 385–6.

The threat of gonorrhoea to the people of the Cameroons was realized in the second half of 1959; during recent years this has been met by instituting a large number of centres staffed by a single orderly provided with a supply of antibiotics and sulphonamides; orderlies also travelled about giving injections of penicillin in the various villages visited. Syphilis was dealt with by a Treponematosis Section of the Service d'Hygiène Mobile et de Prophylaxie, which included yaws as well. Results of all these were excellent.

Unfortunately gonorrhoea soon became more or less resistant to penicillin (in the doses employed) as this and the sulphonamides became saleable.

A 6 months' campaign was inaugurated to carry treatment facilities into 50 areas most affected. This consisted of the following: (1) for acute gonorrhoea 1 gm. dihydrostreptomycin and 5 gm. thiazamide daily (in 2 doses) for 5 days; (2) for chronic gonorrhoea 1 gm. dihydrostreptomycin daily for 5 days plus an intramuscular injection of Propidon [this is not described; the name has been used for a vaccine of staphylococci, streptococci and pseudomonas] on the first, third and fifth days; (3) for syphilis 3 daily intravenous injections of 0·01 gm. cyanide of mercury to prevent reactions, followed after 3 days by 5 weekly injections of 3 mega units of procaine penicillin; (4) for yaws 1·2 mega units of procaine penicillin for adults and 600,000 units for children under 14.

The intention was to bring in as many patients as possible by means of the administrative authorities, leaflets, radio and loud-speaker. Surveillance of prostitutes and their regulation were also attempted. Treatment teams consisted of 5 male nurses, 1 for consultation, 1 for reception, 1 for laboratory tests, 1 for treatment and 1 for taking specimens (of blood etc.) and helping with the treatment; and 1 female nurse, all under the supervision of a medical section chief.

During the second half of 1960 [? first half of 1960] there were treated 12,293 cases of gonorrhoea, 516 of yaws and 674 of syphilis by 12 teams visiting 50 centres.

The customs of the Moslem population caused considerable difficulty but males usually attended well and in one dispensary the women were mostly willing to come for treatment in the evenings from 6 to 9 o'clock. The overall success was considerable and it is hoped to create more dispensaries in addition to those in Douala, Yaoundé and Maroua. *T. E. Osmond*

PREISLER, O. Untersuchungen über die Urogenitaltrichomonase. **[Genito-Urinary Trichomoniasis]** *Deut. med. Woch.* 1960, Dec. 9, v. 85, No. 50, 2185–92, 2225–6. [254 refs.]

This paper contains much interesting information on genito-urinary trichomoniasis together with a very long

list of references of experience in other countries. There is a good summary in English.

In a cancer-prevention survey conducted in a clinic in Freiburg, *Trichomonas* was found in 28% of 901 women during routine vaginal examinations. The incidence of the infection was highest in the lower age-groups—37% at 31–40 years and only 4% over 60 years. 588 (65·3%) of the women complained of a vaginal discharge but in only 212 (36%) of these was a *Trichomonas* infection found. On the other hand in only one-sixth of the cases of trichomoniasis was there a vaginal discharge. In 75% of the cases the organism was also isolated from the urethra and the cervix. A quarter of the husbands of women with trichomoniasis were found to be infected but in most of them there were no symptoms. There was no evidence of carcinogenic action of trichomoniasis. Some of the characteristics of the infecting organism are stated with mention of the fact that it remains viable in chlorinated swimming-bath water for 10 minutes but is destroyed by sea-water within 5 minutes.

The therapy of trichomoniasis is considered at some length with emphasis on the opinion that treatment by antibiotics or therapeutics is not as yet fully effective. Although a primary cure can be secured by either treatment, in a high proportion of cases a permanent cure can be obtained in only about a half of them.

M. E. Delafield

GENERAL INFECTIVE DISEASES

The order in this section is:—**General; Hospital and other Cross Infections; Coccal Infections; Bacterial Infections; Virus Infections.**

GENERAL

SPARKS, J. P. & SMITH, R. E. **Winter Epidemics in a Closed Community.** *Practitioner.* 1960, Dec., v. 185, No. 1110, 754–63, 1 fig.

This is a statistical and general account of the infections which have occurred in Rugby School during the past decade. Most of these have been seen in the Lent term. Influenza and epidemic sore throat are dealt with in some detail. Modern public schoolboys appear to suffer from catarrh very rarely when they have measles. Public schools are more popular than they ever were, and overcrowding is becoming a possible danger to health.

H. Stanley Banks

GEEFHUYSEN, J. & ROSEN, E. U. **Purulent Meningitis in 204 Bantu Children.** *South African Med. J.* 1960, Nov. 19, v. 34, No. 47, 986–93. [54 refs.]

In 204 consecutive cases of purulent meningitis in Bantu children treated in Baragwanath hospital, Johannesburg, organisms found in the cerebrospinal fluid were: pneumococci 54 (26%); *Haemophilus influenzae* 32 (16%); meningococci 49 (24%); others 6 (3%). In 62 cases no organism was found. Tuberculous meningitis was carefully excluded.

A very detailed discussion is given of prognosis, survival and sequelae, in relation to duration of illness before and after admission, condition on admission, and therapy. The following points are only a selection of those discussed. A depressed level of consciousness on admission was always a grave prognostic sign, whatever the causative organism. Malnutrition associated with pneumococcal meningitis was of grave significance. The prognosis was improved if a subdural effusion could be diagnosed and treated early, as others also have found. The occurrence of sequelae was higher in those whose pyrexia persisted for over 10 days, in influenzal meningitis. For pneumococcal meningitis the main treatment was 1 mega unit penicillin intramuscularly every 2 hours, after an initial intrathecal injection, obviating the need for repeated intrathecal therapy. For influenzal meningitis chloramphenicol was the antibiotic of choice: it is suggested that the crystalline form is preferable to the esterized form. Sulphadiazine was the drug of choice for meningococcal meningitis. The patients in whom no organisms were found were treated according to their clinical appearances, with penicillin and sulphadiazine, alone or with streptomycin or chloramphenicol. 69% of them survived. It is considered that such cases are most likely to be pneumococcal, influenzal or meningococcal, having had inadequate treatment before admission.

B. B. Waddy

BECKERS, R. Essais sur des associations de vaccins. [**Trials on Combined Vaccinations**] *Arch. Belges Méd. Sociale, Hyg., Méd. du Travail et Méd. Légale.* 1960, May, v. 18, No. 5, 358–68. [23 refs.]

This paper was originally delivered at the conference on immunization in childhood held in Paris, October 19–21, 1959, and is mainly concerned with the combination of prophylactics in order to reduce the number of injections given to very young children. The tetravalent poliomyelitis-diphtheria-tetanus-pertussis vaccine trial with 200 children of 9 months to 12 years is not reported in detail, but, in common with other investigations of this sort reported at that time, the immune response to Types 2 and 3 poliovirus were superior to that of Type 1.

The paper itself is followed by a report by BECKERS on the conclusions reached by the conference at the Centre International de l'Enfance [this *Bulletin*, 1960, v. 35, 1111].

H. J. Bensted

SOKOLOVA, N. N.; APANASHCHENKO, N. I.; ZHDANOV, V. M. **Experimental Investigations of Influenza-Diphtheria-Pertussis Vaccine. I. Immunological Reaction to Influenza Antigen** [SOKOLOVA, APANASHCHENKO & ZHDANOV]. *Problems of Virology.* London. 1960, v. 5, No. 1, 55–60. [17 refs.] **II. Immunological Reaction to Diphtheria and Pertussis Antigens** [APANASHCHENKO, SOKOLOVA & ZHDANOV]. *Ibid.*, 60–63. [Translated from Russian.]

These two papers record the results in guineapigs of administering 2 subcutaneous doses, with an interval of 3 weeks, of a combined influenza-diphtheria-pertussis vaccine. A killed strain of influenza virus type B with a haemagglutination titre of 847 (or 84·7 in some experiments) was added to purified diphtheria toxoid (30 Lf) and pertussis vaccine (20,000 million organisms per ml.). Parallel experiments were carried out with influenza-diphtheria, diphtheria-pertussis, influenza and diphtheria vaccines. All combinations were used unadsorbed and adsorbed with aluminium hydroxide. The antigenic activity of the adsorbed influenza vaccine was much greater than that of the unadsorbed influenza vaccine: both were 2–3 times less immunogenic than the combined preparations. Combination of the influenza antigen with diphtheria and pertussis components raised its antigenic activity, which also rose with the concentration of the influenza antigen. The influenza antigen did not exert any appreciable suppressive effect on the antigenic properties of the diphtheria and pertussis components.

D. A. Cannon

HOSPITAL AND OTHER CROSS INFECTIONS

KWANTES, W. **An Outbreak of Acute Otitis Media in a Maternity Hospital due to *Pseudomonas pyocyanea*.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, Sept., v. 19, 169–72.

An outbreak of infection due to *Pseudomonas pyocyanea* in a small maternity home during August 1958 is described. During that month 4 infants had acute otitis media, 4 had conjunctivitis and 2 mothers had mastitis due to that organism.

Efforts to find the source of infection included the bacteriological examination of nose and throat swabs of the staff. Examination was made of floor dust, furnishings, infants' toilet articles and dried milk. *Ps. pyocyanea* was not isolated from any of these places although the organism was recovered from 6 of the 11 infants remaining in hospital. [There is no mention of attempts to recover the organism from the napkins.] One member of the domestic staff was also excreting the organism.

The hospital was closed on September 1st and reopened 5 days later after cleaning. No further cases of *Ps. pyocyanea* infection occurred and an investigation into family contacts of mothers in hospital during the epidemic failed to reveal the source of the infection.

M. Patricia Jevons

LIE KIAN JOE, SAHAB, K., GAN-OEI SIOK YAUW & MAKALIWY, C. **Infantile Gastroenteritis in a Newborn Infant Nursery in Djakarta, Indonesia.** *J. Trop. Pediatrics.* London. 1960, Dec., v. 6, No. 3, 67–74.

Infant diarrhoea is endemic in the newborn infant residence of the Central Hospital, Djakarta [this *Bulletin*, 1959, v. 34, 206, *bis.*] and causes considerable mortality, especially among premature infants. The authors describe their bacteriological investigations into this problem, stools being cultured from babies with diarrhoea, and also in a few that did not gain weight, over a period of 6 months from 1 August 1957 to 31 January 1958.

Of 394 babies weighing over 2,000 gm. at birth who stayed in hospital 5 days or more, 96 contracted diarrhoea, and *Escherichia coli* of strains considered to be pathogenic were isolated in 29.

Of 118 babies weighing under 2,000 gm. at birth who stayed or survived 5 days, no less than 115 contracted diarrhoea, and 3 did not gain. From these pathogenic *E. coli* were isolated in the stools of 63 and in the vomit of one.

Of the 93 babies from whom pathogenic *E. coli* were obtained there were 32 who died. All but two of these weighed under 2,000 gm. at birth. This compares with 20 deaths in the 124 cases from which no pathogenic *E. coli* were isolated.

No shigellae or salmonellae were isolated during the survey.

A list of the different serotypes isolated is given. The most frequent and continuously endemic was serotype O111:B4. Other serotypes appeared less able to maintain themselves. The authors consider that more frequent culture would result in an increase in the percentage of stools found to contain pathogenic *E. coli*.

The authors found little evidence for maintenance of infection by carriers among the medical or nursing staff or among the kitchen personnel. They consider that overcrowding and admission of infected infants from home or other hospitals were the main factors involved.

The *E. coli* isolated during this period were sensitive to chloramphenicol and the tetracyclines, and were treated accordingly. Resistance to these antibiotics was found frequently after the end of the period.

A. C. E. Cole

SCHRECK, K. M., with the technical assistance of Emily HOPPS. **Observations on the Epidemiology of Staphylococcal Infections.** *Amer. J. Med. Sci.* 1960, Aug., v. 240, No. 2, 171–85, 11 figs. [11 refs.]

The staphylococcal disease acquired in the author's hospital over a 4-year period (1956–59) was studied. The incidence of infection was only 1·1% of admissions and births over the period (this was assessed on the number of specimens reaching the laboratory from separate patients, from which coagulase positive staphylococci were isolated). During the first 3 years between 57% and 63% of infections were due to strains of phage type 80/81, but in the 4th year strains of this type accounted for 38% of infections.

Surgical patients accounted for about 2–3 times as

many strains as medical patients. There were fewer strains from patients in the maternity unit than in the other departments except in 1956 when 81% of 93 strains were of types 80/81. 73% of 279 lesions in the hospital personnel over the period of investigation were due to strains of this type.

The decrease in 80/81 infections in 1959 was accompanied by an increase in lesions due to other phage types. Strains of 52 other types caused lesions in this year, 18 of them being responsible for 2 or more lesions.

Over 90% of the 80/81 strains isolated in 1959 were resistant to penicillin, streptomycin and tetracyclines and over 70% of them were resistant to erythromycin. Nontypable strains and strains of phage types other than 80/81 tended to be less resistant to the common antibiotics but an increase in resistance to chloramphenicol and novobiocin was demonstrated in the 4th year of the study.

Heavy environmental contamination by type 80/81 could not be demonstrated by air sampling, nasal swabbing or examination of blankets or furniture. The effect of control measures and the probable mode of transmission of the organisms are discussed.

M. Patricia Jevons

NAHMIAS, A. J., GODWIN, J. T., UPDYKE, Elaine L. & HOPKINS, W. A. **Postsurgical Staphylococcic Infections. Outbreak traced to an Individual carrying Phage Strains 80/81 and 80/81/52/52A.** *J. Amer. Med. Ass.* 1960, Nov. 5, v. 174, No. 10, 1269–75, 1 fig. [20 refs.]

A disturbing number of post-operative staphylococcal infections in a U.S. hospital led to a preliminary epidemiological investigation. This demonstrated a particularly high incidence in patients undergoing thoracic surgery and it was then observed that surgeon C had been concerned with all of 13 operations in such patients. Phage typing of staphylococci from 5 patients showed that all were type 80/81. 1 intern had a lesion due to a staphylococcus of the same type; surgeon C carried in his nose and on his skin a mixture of staphylococci of types 80/81 and 80/81/52/52A. Surgeon C was removed from duty and within 3 days, apparently spontaneously, ceased to carry the epidemic strain. For 6 months after his return to duty the infection rate remained very low but then 2 more patients developed infections after thoracic operations and were found to be infected with type 80/81 staphylococci; surgeon C and 2 other members of the team were found to be carriers of staphylococci of type 80/52/52A. Reference is made to recent work on laboratory transformation of staphylococci of these and related phage types [this *Bulletin*, 1959, v. 34, 1174, 1175]. *R. E. O. Williams*

BENHAM, R. S., HAVENS, Isabelle & LANDY, J. J. **Respiratory Flora of Hospital-Related Populations.** *J. Infect. Dis.* 1960, July–Aug., v. 107, No. 1, 1–10, 6 figs.

A number of surveys were made of the nose and throat flora of several groups of surgeons and of a number of other groups of volunteers with varying degrees of hospital contact. 43% of a group of surgeons swabbed in 1952 carried antibiotic-resistant staphylococci and 5% yielded coliforms; in 1958 only 10% of the same group had resistant staphylococci while 24% had coliforms. A similar trend was noted in the percentages of clean surgical wounds yielding the 2 groups of microbes. The frequency of carriage of antibiotic-resistant bacteria—both staphylococci and coliforms—in several groups of volunteers seemed to be related to their closeness of contact with patients. Most of the resistant staphylococci fell into phage group III or were type 80/81 (here classified as belonging to the Miscellaneous Group), or were untypable. The 80/81 strains were particularly common among the relatively few resistant strains from non-hospital sources.

[Assessment of the results is greatly hindered by the fact that they are all presented in percentages without details of the numbers represented in the various subgroups.] *R. E. O. Williams*

WILLIAMS, R. E. O., BLOWERS, R., GARROD, L. P. & SHOOTER, R. A. **Hospital Infection. Causes and Prevention.**

This book was reviewed on p. 211.

COCCAL INFECTIONS

The order in this section is:—***Staphylococcus, Streptococcus, Neisseria, Others.***

FORSEY, R. R., ARENDT, E. C., DEVRIES, Joan & THOMPSON, A. **Prophylaxis against Staphylococcal Infection among Nurses in a General Hospital.** *Canadian Med. Ass. J.* 1960, Nov. 19, v. 83, No. 21, 1108–9.

124 nurses entering a general hospital in Canada were given monthly doses of a heat-killed vaccine prepared from 3 strains of *Staphylococcus aureus*. 122 nurses were kept as controls [but the method of selection is not discussed]. After follow-up periods of 9–21 months, 18 staphylococcal infections were recorded in the vaccinated group compared with only 9 in the corresponding controls. *R. E. O. Williams*

DEARING, W. H. & NEEDHAM, G. M. **Hospitalised Patients with *Staphylococcus aureus* in the Intestine.** *J. Amer. Med. Ass.* 1960, Nov. 19, v. 174, No. 12, 1597–602. [16 refs.]

This is a study of staphylococcal intestinal infection in 243 patients whose stool cultures revealed *Staphylococcus aureus*, between April 1958 and March 1960 in

the Mayo Clinic, Rochester, U.S.A. No epidemic of intestinal infection is involved but the figures show that symptomatic staphylococcal intestinal infections keep on occurring in the wards in spite of continuous measures to prevent them. The number of staphylococci present in the faeces has some relation to the severity of the symptoms but this is not complete—when few are present, symptoms are usually mild but when many are present symptoms may range from mild to very severe. Many important problems are not solved, for example the relationship of staphylococcal enteritis to pseudomembranous enterocolitis and the danger of spread to other sites on the patient's body or to other patients. Staphylococcal enteritis is usually reversible by the use of the appropriate antibiotic and no deaths were shown to be due solely to staphylococcal enteritis. This does not apply to pseudomembranous enterocolitis which is usually fatal. The ability of the staphylococcus to produce enterotoxin may be the factor connecting simple staphylococcal enteritis with pseudomembranous enterocolitis but biological tests on kittens and monkeys are not precise or specific enough to determine whether a given staphylococcus produces a potent enterotoxin or not. Surgical patients given pre-operative antibiotic prophylaxis are more liable to suffer from staphylococcal enteritis than others not so treated. With the use of such prophylaxis as a routine, hospital staphylococci tend to become resistant to the antibiotics used, including neomycin and bacitracin. [This is a most important article on a subject full of difficulties; it requires careful study.]

[See also this *Bulletin*, 1953, v. 28, 734; 1955, v. 30, 1110.] *A. B. Christie*

RUTENBURG, A. M., GREENBURG, H. L. & SCHWEINBURG, F. B. **Clinical Experiences with 2, 6-Dimethoxyphenyl Penicillin Monohydrate in Staphylococcal Infections.** *New England J. of Med.* 1960, Dec. 8, v. 263, No. 23, 1174–8. [11 refs.]

The authors tested 100 strains of staphylococci for *in vitro* sensitivity to penicillin G and to dimethoxyphenyl penicillin (Celbenin). 98 of the strains were sensitive to 6·3 μgm. or less per ml. of dimethoxyphenyl penicillin: 93 of the 98 were resistant to penicillin G at concentrations of 4 or more units per ml.: 5 strains were more sensitive to penicillin G than to dimethoxyphenyl penicillin. There was no relation between the sensitivities to the two drugs nor did the size of inoculum have any effect on the minimum inhibitory concentration of dimethoxyphenyl penicillin. 41 patients suffering from staphylococcal infections, 31 of whom had not responded to other antibiotics, were treated successfully with dimethoxyphenyl penicillin. After 1 gm. of the drug intramuscularly, serum concentrations of 7·3 to 15·0 μgm. per ml. were obtained after 1 hour, 1·2 to 3·8 μgm. after 4 hours, and less than 0·5 μgm. after 6 hours. Tubular blocking agents such as probenecid increased serum concentrations and prolonged penicillinaemia. There were no side effects and no resistant strains of staphylococci were encountered. *A. B. Christie*

BRUCE, L. G. & GIBSON, G. L. **Erythromycin Propionate in the Treatment of Staphylococcal Infection.** *Scottish Med. J.* Glasgow. 1960, Dec., v. 5, No. 12, 523–5.

The authors treated 12 patients suffering from staphylococcal infections with erythromycin propionate, 250 mgm. orally every 6 hours for 1 or 2 weeks. In no case did the serum erythromycin level fall below 8 times the minimum necessary to inhibit the growth of the staphylococcus. With even this level, in 4 cases the drug did not reach the organism in sufficient strength to destroy it. 5 patients had post-operative infection of chest spaces—1 was cured and the other 4 had some temporary improvement. Of 7 patients with acute infections there was only 1 case of complete bacteriological failure. The authors feel this drug has a useful place in the treatment of penicillin-resistant staphylococcal infection. *A. B. Christie*

STRATFORD, B., RUBBO, S. D., CHRISTIE, R. & DIXSON, Shirley. **Treatment of the Nasal Carrier of *Staphylococcus aureus* with Framycetin and other Antibacterials.** *Lancet.* 1960, Dec. 3, 1225–7, 2 figs.

Nasal carriage of *Staphylococcus aureus* was determined by a "deep nasal swab", *i.e.* a swab inserted into the nasal fossa to a point just below the middle turbinate. 103 hospital patients were swabbed by this method and by a conventional technique in which only the nasal vestibule was swabbed. 51% of the deep swabs yielded *Staph. aureus* compared with only 34% of the anterior nose swabs. [MOSS *et al.* (this *Bulletin*, 1948, v. 23, 452) found the reverse difference when deep nasal swabs were taken with precautions to avoid contamination from the vestibule.]

Each of 20 persons found to be nasal carriers of *Staph. aureus* was treated with 1 or other of 6 antibacterial preparations. The best was a Soframycin (framycetin and gramicidin) spray with a vasoconstrictor, administrated once daily; this cleared 17 of the carriers in 24 hours and all 20 by 7 days. Soframycin ointment twice daily gave only 25% and 90% respectively, and Naseptin [Hibitane and neomycin] ointment only 5% and 45% clearance. The average time for recolonization after Soframycin spray was 14 days, compared with 2 days after Naseptin ointment.

[RAMMELKAMP, in a letter in the *Lancet* (1961, v. 1, 112) mentions that microconsolidation of the lung has been observed in animals inhaling gramicidin.] *R. E. O. Williams*

EHRENKRANZ, N. J., COHEN, H. & ROMERO, Aida. **The Clinical Evaluation of Vancomycin in Treatment of Multiantibiotic Refractory Staphylococcal Infections. II. The Use of Vancomycin after Failure of Bactericidal Antibiotics.** *Arch. Intern. Med.* 1960, Dec., v. 106, No. 6, 842–51

"In order to measure the relative usefulness of vancomycin in the therapy of staphylococcal infections, nine

patients were treated with this antibiotic after their infections were found to be clinically, but not bacteriologically, refractory to another bactericidal drug. Six were cured by the administration of vancomycin. In addition to being superior to bacteriostatic antibiotics, vancomycin appears to be more effective than kanamycin for the treatment of staphylococcal infections. The relative merits of vancomycin, penicillin, and ristocetin need further study."

CARROLL, G., GIBAS, D. & KARELLOS, D. **Triacetyloleandomycin with Triple Sulfa. Its Role in the Control of *Staphylococcus* and *Streptococcus* Infections in the Urinary Tract.** *J. Amer. Med. Ass.* 1960, Nov. 19, v. 174, No. 12, 1603–5.

Patients with urinary infections due to antibiotic resistant organisms were treated with a combination of triacetyloleandomycin and tri-sulphonamides. Tablets containing 75 mgm. of the former and 111 mgm. each of sulphadiazine, sulphamerazine and sulphamethazine were given in a dosage of 2 tablets 3 times a day for 5 days. The authors claimed success in a variety of urinary infections due to either staphylococci or streptococci. [The figures are difficult to follow. A total of 273 patients is mentioned in the text, 277 in the summary but the figures appear to add up to 276: of 113 patients, 86 are said in the text to recover, yet the figures shown in the tables are 64 and 17.] *A. B. Christie*

ŠRÁMEK, J. **Some Factors influencing the Incidence and Spread of Streptococcal Infections in the Population of a Small Village.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 3, 300–306. [17 refs.]

This paper was presented at the International Epidemiological Symposium in Prague in February 1960.

Investigation was made over the period 1954–59 of the incidence and spread of streptococcal infections in a village of about 340 persons. A table sets out the annual number of clinical cases, the total of which in the whole period was 15 scarlet fever, 221 sore throat, 4 cervical lymphadenitis, 3 rheumatic fever and 1 erythema nodosum. Bacteriological and serological examinations were carried out in a considerable proportion of these patients. In addition about 5,000 nose and throat swabs were taken for examination on 23 occasions from schoolchildren and 9 times from the general population in the course of the 5 years. From these swabs 776 strains of β-haemolytic streptococci were isolated and of these 461 (59%) belonged to Lancefield Group A. Typing of these Group A strains was carried out and 15 different serotypes were discovered.

The results are described, set out in tables and discussed, with the conclusion that the introduction of a virulent streptococcus of a serological type not previously experienced in the population was the main factor in causing a high incidence of streptococcal diseases. The mass observation of the population indicated an exchange of the different serotypes during the 5 years. As a rule only during the first period of spread of a particular type was infection accompanied by typical illness.

Reference is also made to the important part played by children at the local school in causing spread of infection to the general population. Mention is made of the value of the administration of penicillin to all children at school in times of epidemic in lessening the further spread of infection. *M. E. Delafield*

KIRBY, J. C., Jr., POLIS, G. & ROMANSKY, M. J. **A Controlled Blind Study of Pneumococcal Pneumonia treated with Tetracycline and Tetracycline plus 6-Methyl Prednisolone.** *Amer. J. Med. Sci.* 1960, July, v. 240, No. 1, 30–35, 1 fig. [10 refs.]

The authors treated 2 groups of patients suffering from pneumococcal pneumonia, one with 2 gm. of tetracycline daily for 5 days, the other with the same antibiotic plus 6-methyl prednisolone, 32 mgm. on the first day, 16 mgm. on the second and third day and 8 mgm. on the fourth day. Fever fell more quickly in the group receiving 6-methyl prednisolone but there was no other difference between the two groups. The authors conclude that there is no indication for the use of corticosteroids in uncomplicated pneumococcal pneumonia though they might be useful in highly febrile and toxic patients. *A. B. Christie*

HOAGLAND, R. J., BARTELLONI, P. & CATALDO, J. R. **Meningococcemia: a Cause of Prolonged Fever.** *U.S. Armed Forces Med. J.* 1960, Oct., v. 11, No. 10, 1190–94.

This is a description of a case of chronic meningococcaemia in a soldier aged 22. The symptoms were recurring febrile episodes along with a maculo-papular rash and swelling of the ankles. Most of the macules were about 1 mm. in diameter, a few up to 4 or 5 mm. and some became purpuric. The patient was eventually treated with corticosteroids and responded but when results of blood cultures became known he was treated with massive doses of penicillin. Differential diagnosis is discussed. [Chronic meningococcaemia was seen frequently in the early years of the last war: it responded rapidly to sulphonamides. It is rarely diagnosed nowadays, possibly, as the authors suggest, because febrile conditions are so often treated with antibiotics before a diagnosis is made.] *A. B. Christie*

BACTERIAL INFECTIONS

The order in this section is:—***General, Corynebacterium, Haemophilus, Enteric bacteria, Brucella, Pasteurella, Bacillus, Anaerobes, Spirochaetes, Others.***

BHATTACHARJI, L. M., SEN, P. C., SANYAL, B. C. & TALAPATRA, N. C. **Diphtheria. An Epidemiological Study at Singur, 1958–1959.** *Alumni Ass. Bull.* Calcutta. 1960, Apr., v. 9, No. 15, 21–7.

This is a study of the incidence of diphtheria in the Unions of Singur, West Bengal, in the 3 years 1957–59.

There appeared to be a considerable increase in the disease during the period though some of this was probably due to improvement in reporting and diagnosis. That diagnosis is still inaccurate is shown by the mortality figures—14·81% in 54 cases of bacteriologically proved diphtheria in the age-group 1–3 years, but nil in 84 cases diagnosed clinically in the same age-group. The authors feel that the incidence of the disease in the area is of the same order as obtained in England and Wales before mass immunization and that a campaign for immunization in the area is justified. *A. B. Christie*

Bhargava, H. S. & Bhatt, A. N. **A Study of 275 Cases of Diphtheria.** *J. Indian Med. Ass.* 1960, Sept. 16, v. 35, No. 6, 243–8.

Diphtheria is still a common and severe disease in India. This detailed clinical analysis of 275 cases reported from Nagpur recalls the disease as it existed in Western countries before the era of active immunization, but there are certain differences. The maximum incidence was in lower age-groups—1 to 2 years (29%), 2 to 4 years (20%) and under 1 year (17·9%); and above the age of 12 years there were only 6 cases. As many as 35% of the patients suffered from dyspnoea (many with pneumonia), thus indicating a very high proportion of laryngeal cases. The total mortality was also high (20%) and among laryngeal cases very high (46·4%).

Treatment with antitoxin seemed to be adequate but not as effective as it should have been. After-care may have been deficient—there were 28 cases of cardiovascular failure; the small incidence of paralysis was misleading, and probably due to the discharged patients not reporting back for examination. The authors blame the poor nutritional state of the mothers and infants, and the lack of active immunization in early infancy for these results. No bacteriological data are given.

H. Stanley Banks

Bokkenheuser, V. & Smith, A. H. **Trends in Prophylactic Diptheria Immunization in Johannesburg.** *South African Med. J.* 1960, Oct. 29, v. 34, No. 44, 928–34, 2 figs. [28 refs.]

In South Africa diphtheria has been endemic for many years [this *Bulletin*, 1944, v. 19, 578] and, at least up to 1952, there were no signs of a decline in the morbidity rate [*ibid.* 1955, v. 30, 8]. The disease is particularly frequent in Johannesburg, with the highest incidence in the white population. A critical examination was therefore made of the system of prophylactic immunization in force in Johannesburg among white, Asian, and coloured children born between 1950 and 1957. By means of questionnaires it was found that a primary course of immunization had been given to children 1–7 years of age in 99·1% in the highest social class, and to 40% or less in the poorer classes, including the poor whites, the Asians, and the coloured. The Bantu population could not provide the requisite information. These immunization rates, directly related to the socio-economic standard, are grossly inadequate for elimination of the disease in all three sections of the population; moreover, booster injections are almost ignored.

Measures suggested for improvement of this unsatisfactory situation include better teamwork on the part of family doctors, health visitors, district nurses, staffs of welfare centres, and voluntary workers, at first directed towards public education. The introduction of a card system by health visitors to newborn children is specially recommended. One form of such a card has 3 squares, each of which can be detached and is valid for an immunization dose free of charge when presented to a doctor, and also for repayment of the doctor's fee when presented by the doctor to the local authority. The municipal immunization clinics also need to be strengthened.

[See also this *Bulletin*, 1956, v. 31, 792, 885.]

H. Stanley Banks

Islam, N. & Haq, A. Q. M. N. **Chloramphenicol in Typhoid Fever—a Reduced Dosage.** *Southern Med. J.* 1960, Oct., v. 53, No. 10, 1291–5. [14 refs.]

The dosage of chloramphenicol in typhoid fever has tended to become standardized at about 3 gm. daily for adults until the temperature falls, and a reduced dosage thereafter for a few days. An initial loading dose of 2–4 gm. was at first recommended, but later was often omitted because of the occurrence of Herxheimer-like reactions. The high cost of the drug is a severe burden in some countries, and this article from East Pakistan describes an investigation to determine a minimum effective dose schedule. The number of people studied was 200, in 4 groups of 50 (all over 10 years of age).

The loading dose in all cases was 500 mgm. and then a dose of 250 mgm. was given in all cases, but at intervals of 2, 3, 4, and 6 hours respectively in the 4 groups. This was continued until the temperature fell to normal, when the time interval between doses was lengthened to 6 hours in all groups except the first, where it was changed to 4 hours. The results were practically similar in all groups, as judged by the day of response to the drug (average 4 days), and the number of relapses (6–10%). The 4 deaths among the 200 cases (all from perforation and shock) were distributed at random among the groups, and seemed unrelated to dosage. The 7 cases of intestinal haemorrhage were also randomly distributed. The conclusion from this investigation was that an initial dose of 0·5 gm., followed by 1 gm. daily until 4 to 7 days after the temperature becomes normal, is as effective as larger dosage schedules, and considerably cheaper.

H. Stanley Banks

Rodríguez-Leiva, M. ***Escherichia coli* Studies. VII. Incidence of Enteropathogenic *Escherichia coli* in the Acute Diarrhea of Infants in Santiago, Chile.** *Amer. J. Hyg.* 1960, Sept., v. 72, No. 2, 162–8, 4 figs. [27 refs.]

This is a report covering a period of 4 years on 1,650 infants admitted to a children's hospital with acute diarrhoea, fever, vomiting and dehydration. About 7% were prematures and 93% showed evidence of malnutrition; the ages ranged from 1 day to 2 years, with an average

of 4·6 months. Enteropathogenic *Escherichia coli* were present in 23·8% of this group of patients. The patients came from an open community and the seasonal distribution corresponded to a spring-summer infection. Over 80% of the isolations were from infants under 6 months of age. *E. coli* O111 was the most common type and accounted for half the strains isolated, with O26 and O55 coming second and third in order of frequence. Types O127, O86 and O128 were the only other types identified and these were rarely isolated. *H. J. Bensted*

Mushin, Rose, Lowson, Frances M. & Bishop, Ruth F. **Bacteriological and Epidemiological Studies on Coliform Diarrhoea in Children.** *Med. J. Australia.* 1960, Sept. 3, v. 2, No. 10, 365–72, 2 figs. [41 refs.]

There were 1,122 babies, mostly under the age of 1 year, in this survey which included control groups totalling about 10% of the whole; its aim was to assess the incidence and epidemiological importance in Melbourne of 14 *Escherichia coli* serotypes: O26; O55; O86; O111; O18; O119; O125; O127; O128; O25; O44; O112; O124; O126. Some of these types were widely accepted as pathogens while there was considerable doubt about the aetiological role of others. The survey also covered the incidence of salmonella and shigella organisms.

The highest incidence of enteropathogenic *E. coli* was found in institutions other than hospitals, where the isolation rate averaged from 20 to 30% and *E. coli* O26; O55; O86 and O111 formed 85% of the *coli* isolations. Of the other serotypes O18 was found in 9 babies, O126 in 4 and O44 and O128 in 2 each; the other 6 serotypes were not encountered. The greatest incidence of salmonella and shigella infections was found among the gastro-enteritis cases in a children's hospital; *Salmonella typhi-murium* and *Shigella sonnei* were the types most frequently isolated.

There was no suggestion that adult contacts were important sources of infection and there was little doubt that symptomless excreters and sick babies were responsible for institutional cross-infections. The results of this survey would agree in general with the observations of other workers. *H. J. Bensted*

Bachrach, U., Sterk, V. V., Gery, I. & Rozansky, R. **Volatile Amines in Stools of Infants suffering Gastroenteritis.** *Amer. J. Hyg.* 1960, July, v. 72, No. 1, 1–5, 1 fig. [15 refs.]

It was found that the stools of 21 infants out of a total of 26 suffering from gastro-enteritis of unknown origin contained a volatile amine—phenylethylamine—which disappeared from the stools after recovery from the disease. None of the Gram-negative or Gram-positive bacilli cultivated under aerobic or anaerobic conditions from the stools of gastro-enteritis patients or healthy infants produced volatile amines resembling those found in the stools of the patients referred to above. It was, however, found that strains of *Streptococcus faecalis* isolated from the stools of sick infants could produce relatively large amounts of phenylethylamine and tyramine by decarboxylation [this *Bulletin*, 1952, v. 27, 1067]. *H. J. Bensted*

Martin, W. J. Schirger, A., Kelly, P. J. & Beahrs, O. H. **Brucellosis.** *Proc. Staff Meetings Mayo Clinic.* 1960, Nov. 23, v. 35, No. 24, 717–27. [30 refs.]

A general account.

Puntigam, F. Erkrankungen an thorakalen Formen der Tularämie bei Arbeitnehmern in Zuckerfabriken. **[Tularaemia in Workers in Beet Sugar Factories]** *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 147, No. 2, 162–8, 3 figs.

No reports on tularaemia in workers in sugar factories seem to have been published hitherto in the German and English literature although such infections have been recorded in Russia where an associated increase in the numbers of field mice which had gained entrance to the sugar beet was shown to have occurred.

Here described is an outbreak of an influenzal type of illness among the workers in a sugar beet factory employing 830 men and 198 women in the south east of Lower Austria. It began in early November 1959, continued through the succeeding weeks and rose to a peak at the turn of the year, after which the epidemic gradually subsided.

All patients had fever of 39°–40° C. often followed by a remission and a second rise in temperature. The main symptoms were frontal headache, lassitude and muscular pains round the chest which caused great difficulty in breathing. There were no catarrhal symptoms. In a few patients there were the secondary effects of the appearance of an erythematous rash and signs of meningeal and encephalitic irritation. Chest X-ray examinations revealed considerable increase in size of the hilum, and atypical pneumonia. The blood sedimentation rate was much increased and there was a leucocytosis of about 10,000. There were no deaths.

The infections occurred throughout the period when sugar beet was being washed before processing. It is considered that the infection was by droplets from the wash water from the beets grown in a district where tularaemia is endemic in field mice which had increased greatly in numbers.

Serological investigations carried out after the beet washing period on over 700 employees showed that in about 80% there was an agglutinin titre of tularaemia organisms of over 1 in 50. 85 of these workers giving a positive agglutination test had not reported sick during the beet washing period which suggests that they had had the infection at a previous date.

Blood investigations carried out on workers in the 6 other sugar factories in Austria showed that in 5 of these there was a greater or lesser degree of tularaemia infection. The tularaemia-free factory obtains its sugar beet from a non-infected district. *M. E. Delafield*

ROSS, Constance A. C. & IVES, J. C. J. **Serological Diagnosis in Leptospiral Aseptic Meningitis.** *Lancet.* 1960, Dec. 10, 1278–9. [10 refs.]

During the 2-year period May 1958–May 1960, sera were obtained from 250 patients with abacterial meningitis (*i.e.* cases of non-paralytic illness with pleocytosis of the cerebrospinal fluid from which no bacteria were isolated). Paired sera were obtained from most of the patients and were examined by a microscopic agglutination test with living antigen suspensions (*L. icterohaemorrhagiae* Wijnberg and *L. canicola* Aldgate) as well as by complement fixation (CF). The CF test was carried out in plastic plates and the antigens used were obtained by boiling cultures of the same 2 strains of leptospires (Terzin's method).

Evidence of leptospiral infection was found in 13 patients (5·2%); this indicates that serological examination for leptospirosis is of considerable value in abacterial meningitis. None of these 13 patients had jaundice or other clinical signs of leptospirosis. Assuming that the highest titre obtained during the course of the illness is given by the infecting type-strain, then *L. canicola* was the responsible organism in 12 cases.

The authors conclude that the CF test was as specific as the agglutination test and that it might be more reliably type-specific in the early stages of illness.

L. H. Turner

COGHLAN, Joyce D. & NORVAL, J. **Canicola Fever in Man from Contact with Infected Pigs. Further Observations.** *Brit. Med. J.* 1960, Dec. 10, 1711–13.

Outbreaks of leptospirosis, caused by *Leptospira canicola,* in workers on pig farms in Edinburgh have been reported by SEILER and the present authors [this *Bulletin,* 1956, v. 31, 1007]. The same authors [COGHLAN *et al., ibid.,* 1957, v. 32, 440] found that apparently normal pigs could harbour the organism; that 19 out of 47 persons in a group of piggery workers had been infected at some time; and that, in 2 farms where some of these people worked, there was serological evidence of past or current *L. canicola* infection in about 50% of the pigs (titres of 1:100 or higher).

The present report deals with 16 other human cases of *L. canicola* infection in the Edinburgh area: 11 of these persons were pig-farm contacts; all except one required hospital treatment and presented with the meningeal non-jaundiced form of leptospirosis; the other had a subclinical infection. The diagnosis was based on a rise in the leptospire-agglutinating titre of the serum and the maximum titres were high (over 1 in 3,000 with living antigen suspensions).

In this series, 5 pig farms were implicated and the infection rates in the pigs (based on agglutination titres of 1:1,000 or higher) were: 9 out of 25, 9/11, 12/12, 24/73 (33%), and 35/44 (80%). Leptospires were seen by dark-ground microscopy of urine in 7 out of 10 random samples. *L. canicola* was isolated by inoculating hamsters with untreated pig urine and also by direct culture of kidney tissue (obtained at the abattoir).

A few pigs were chosen at random on the 2 farms where the earlier outbreaks had occurred: agglutination titres of 1:1,000 or higher were found in 11 out of 13 in one group and in 9 out of 10 in the other.

These findings, with the earlier ones, indicate that in Scotland the pig is an effective reservoir of *L. canicola,* that the infection tends to be maintained in piggeries, and that there is a considerable risk of human cases resulting from contact with contaminated pig urine—especially in young persons newly employed in tending infected animals.

It is possible that a situation similar to that exposed by the authors' work occurs in other parts of the country. Investigations of pig herds are recommended.

L. H. Turner

KOLOCHINE-ERBER, B. & MAILLOUX, M. Les leptospiroses porcines en France. Seconde enquête et isolement de *Leptospira pomona.* [**Porcine Leptospirosis in France. Second Survey and Isolation of *Leptospira pomona***] *Ann. Inst. Pasteur.* 1960, Sept., v. 99, No. 3, 359–75, 1 fig. [41 refs.]

The first survey of porcine leptospirosis in France, published in 1950 [see this *Bulletin,* 1951, v. 26, 148] was based on only 172 sera, obtained from abattoirs; and too few antigens were used. Between 1952 and 1957 a second more extensive survey was made on a total of 1,347 swine sera of which 286 (21·3%) were positive: the details are presented in this paper.

The incidences of the predominant serotypes represented in the 286 positive sera were: *Leptospira pomona,* 43% (125); *L. icterohaemorrhagiae,* 34% (98); *L. mitis* (=*hyos*), 4·8% (14); *L. pyrogenes* Zanoni (=*australis B*), 4·0% (12); *L. canicola,* 3·8% (11); *L. grippotyphosa,* 2% (6); the following were less than 2%—*L. ballum* (4); *L. pyrogenes* Salinem (2); *L. bataviae* (1) and *L. australis A* (1); and 4% (12) were indeterminate.

The locality of origin was known for 1,110 of the pigs. The seropositivity rates for 11 regions covered in this study were: Ile de France, 17% (68/406); Poitou, 9·5% (8/84); Vendée, 27% (50/185); Nantaise, 4% (3/70); Bretagne (part), 17·8% (22/123); Mayenne, 15% (9/58); Normandie and Bretagne (part), 24% (15/62); Picardie, 48% (28/58); Franche-Comté, 50% (18/36); Haute-Savoie, 64% (9/14); Bourgogne, 43% (6/14). These, added to earlier findings, indicate that porcine leptospirosis is widespread throughout France.

Coagglutinins were found in many sera and in most of these groups; often several serotypes were represented, but in some instances a particular serotype predominated in a region. Thus coagglutinins for *L. australis B* (Zanoni) were among the commonest, especially in Ile de France, Mayenne, and Normandie. Occasionally coagglutinins to two or more serotypes were present to the same high titre; as in the 12 "indeterminate" sera mentioned above.

The authors discuss the possible significance of coagglutinins and the apparent association of serotypes of leptospires [with certain localities?] and suggest that their presence may be determined by the local microclimates which would favour some and not others.

The kidneys of 27 pigs were examined histologically and by culture. One was positive (*L. pomona*) and a

focus of leptospires was seen in one block of kidney tissue stained by the Levaditi method. *L. H. Turner*

BESSEIGE, H., RIGAUD, J. L. & FOUROUS, E. A propos d'une épidémie familiale de leptospirose. [**A Family Outbreak of Leptospirosis**] *Bull. Soc. Path. Exot.* 1960, May–June, v. 53, No. 3, 404–7.

A man and his wife, with the younger of their two sons, left Saigon for a week-end holiday on a rubber estate where they walked about among the trees; but they did not bathe in any streams.

After 15 days the man became febrile and *Plasmodium falciparum* was found in his blood; 2 days later the wife sickened (negative blood film), and on the next day the son also had fever. The man's symptoms responded to treatment with "quinoforme" [quinine formate] and "tifomycine" [chloramphenicol].

The illness of all 3 persons was characterized by fever, albuminuria and, on days 3–4, by enlargement of the superficial lymph nodes, and a fleeting rash. The nodes were mobile, not tender, and showed no tendency to suppuration. The rash consisted of lenticular rosy spots —discrete, not itchy, and with no desquamation—distributed over the face, neck, torso and arms.

The man was admitted to hospital where he was treated with penicillin and "hexadécadrol" [dexamethasone] and rapidly improved. The boy received similar treatment at home. The wife continued to look after the house and to nurse her son while neglecting her own treatment. The boy recovered rapidly; the woman much more slowly.

In all 3 persons the following diagnostic procedures were negative: blood culture [*sic*], Paul-Bunnell test, Widal and Weil-Felix tests. Leptospiral agglutination results: man, negative; boy, positive at 1 in 10; wife, positive at 1 in 1,000.

The authors conclude that the diagnosis of leptospirosis was clear in the case of the woman; they deduce that the man and son also had leptospirosis (in view of the similar clinical symptoms) but that early antibiotic therapy had suppressed the development of agglutinins. [More information concerning this possible effect is required.]

Leptospirosis presenting with lymphadenopathy and rash is not common. [The incidence of enlarged lymph nodes given in various other reports is summarized (range 15–50%; commonly about 15–20%) but the references are not given.] Enlarged nodes may be a feature of canicola fever. *L. H. Turner*

COMBIESCO, D., STURDZA, Nina, SEFER, M. & KLIPPER, A. Évolution des agglutinines dans les leptospiroses humaines. Valeur de la réaction d'agglutinationlyse dans la détermination du type étiologique. [**The Course of Agglutinin Formation in Human Leptospirosis. The Value of the Agglutination-Lysis Reaction for Type Determinations**] *Arch. Roumaines Path. Expér. et Microbiol.* 1960, June, v. 19, No. 2, 201–9, 3 graphs.

Agglutination-lysis serological tests, in which numbers of antigenically distinct serotypes of *Leptospira* are used as antigens, do not always provide conclusively diagnostic results. Even in cases proved by isolation of leptospires the serological tests may reveal (1) no demonstrable agglutinins, (2) agglutination at a low titre below a diagnostic level, (3) agglutination with several serotypes at the same titre, or (4) that the highest titre is elicited with a serotype other than the one isolated. [The term "paradoxical" is usually restricted to the last of these 4 types of reaction, but the authors also include the third, see below.]

Sera from 261 patients with clinically diagnosed leptospirosis were studied by serial agglutination-lysis tests in an attempt to determine the pattern of development of agglutinins and co-agglutinins and thereby to estimate the value of such tests as a means of identifying the causal serotype. Since few attempts were made to isolate the responsible organism, the infecting serotype was assumed to be that which gave the highest titre in the latest serum of each patient. On this basis, the incidence of infecting serotypes was: *L. pomona*, 205; *L. canicola*, 24; *L. icterohaemorrhagiae*, 17; *L. sejroe*, 8; indeterminate, 7. Suspensions of *L. grippotyphosa* and *L. biflexa* (Patoc) were also used as antigens.

The time at which agglutinins appeared could be broadly traced from the increase in the seropositivity rates, which were stated to be: days 3–5, 6·25%; days 6–7, 64·1%; days 8–11 92·8%; days 12–14, 99·2%; day 15 on to the end of the 2nd month, 100%. [The extent to which agglutination with *L. biflexa* influenced these rates is not made clear.]

Paradoxical reactions [see above] were common and the incidence [%], by periods from the onset of illness, was: 1st week, 23·7; 2nd week, 26·4; 3rd week, 15·7; 4th week, 19·4; 2nd month, 18·0; 3rd to 6th months, 10·4; 7th to 12th months, 17·5. These figures include reactions with *L. biflexa* but, if these reactions are excluded, the corresponding rates were: 2 out of 26 (7·7%), 19/273 (6·9%), 3/152 (2%), 2/52 (3·8%), 4/61 (6·6%), 1/67 (1·4%), and 3/40 (7·6%).

Several points are discussed. (1) Seropositivity rates would probably have been higher had serum dilutions lower than 1 in 100 been used. (2) Variations in titre (even to the extent of reversion to negative followed by reappearance of agglutinins) were observed in 5 cases: these are difficult to explain, but variations in "sensibility of the [antigens] used" are probably concerned, as was suggested by BORG-PETERSEN and FAGRAEUS [this *Bulletin*, 1952, v. 27, 252]. (3) The responsible serotype [it is claimed] could be determined from serological tests in about 90% of cases in the present series; but the incidence of paradoxical reactions increases as more serotypes are used as antigens. Other authors have found that the results of agglutination tests may not accord with the serotype of leptospire isolated from the patient: in 10·8% of cases in one series [ALEXANDER *et al.*, *ibid.*, 1958, v. 33, 702] and in 9 out of 23 cases in another [ZAHARIJA, *ibid.*, 1958, v. 33, 231]. (4) Agglutination with *L. biflexa* (Patox strain) occurred with the sera of more than 60% of the patients; sometimes this serotype was the only one which reacted, and coagglutinins often appeared early, as KMETY also observed [*ibid.*, 1958, v. 33, 658].

These observations suggest the necessity for further studies of the antigenic characteristics of saprophytic

leptospires and of their significance in the serology of leptospirosis in man and animals [see FUZI and CSOKA, p. 402]. *L. H. Turner*

BEEN, T. E., CLARK, B. M., GRANT, L. S. & BROOM, J. C. ***Leptospirea kremastos* Infection in Jamaica, West Indies.** *West Indian Med. J.* 1960, Mar., v. 9, No. 1, 25–30, 1 fig.

Isolation of *Leptospira kremastos* [this *Bulletin*, 1959, v. 34, 389] for the first time in Jamaica (and, as far as is known, in the western hemisphere) is reported. This (SB) strain was obtained from the blood of a boy 17 years old, on the 4th day of a febrile illness.

The sera of patient SB and others in Jamaica from whom *L. kremastos* has been isolated show cross-agglutination reactions with *L. icterohaemorrhagiae* and with *L. canicola* to titres as high as, or even higher than, the homologous serotype.

The course of leptospirosis due to *L. kremastos* in Jamaica is clinically severe and sometimes fatal [in contrast with observations in Australia]. The salient clinical features in the illness of SB were: febrile onset with severe aching lumbar pain which later extended up to the back of the neck and on over the head; attacks of central abdominal aching pain during the first 2 days; constipation; dark urine, and icteric sclerae (day 3); a few red cells and moderate amounts of albumin, bilirubin, and urobilinogen in the urine; and (day 4) blood-tinged sputum (no abnormal pulmonary and cardiac signs).

Treatment included antibiotics. Achromycin [tetracycline] 1 gm. every 4 hours for 2 doses (the first given intravenously in 500 ml. 5% glucose) was superseded by Chloromycetin [chloramphenicol] (500 mgm. every 4 hours) for about 4 doses before this was stopped (day 5) and Achromycin was recommended until a full course of 30 gm. was given. The patient's condition showed no improvement until Achromycin was recommenced after which the temperature fell to normal within 6 hours, and remained normal. All symptoms and signs had cleared by day 13 and the patient was discharged 4 days later.

L. icterohaemorrhagiae is the only other serotype to have been isolated in Jamaica where the first proved case of leptospirosis was discovered in 1953. Many clinical cases have since been diagnosed and work is in progress to determine the epidemiological patterns of leptospirosis in human beings and in animals. *L. H. Turner*

GOLEY, A. F., ALEXANDER, A. D., THIEL, J. F. & CHAPPELL, V. E. **A Case of Human Infection with *Leptospira mini georgia*.** *Pub. Health Rep.* Wash. 1960, Oct., v. 75, No. 10, 922–4, 1 chart. [10 refs.]

The infectivity of *Leptospira mini*, subserotype *georgia*, has not yet been established for domestic animals or man. The present account, of an accidental laboratory infection in a man aged 53 years, is therefore interesting.

After a long incubation period of 25 days there was a sudden onset of chilliness followed by fever and severe frontal headache and, in the next 36 hours, by generalized muscular aching and mild nausea. Chills recurred every 2–3 hours and the temperature rose to 103·4° F. The patient was first seen on day 2 when he appeared acutely ill: his chest was clear and he had no palpable lymph nodes. Moreover, he had no scleral icterus, conjunctival injection, neck rigidity, liver tenderness, or rash.

Treatment with Aureomycin [chlortetracycline] was given in doses of 500 mgm. orally every 6 hours from early on day 3 until day 8. For the first 48 hours the patient's condition remained the same except that the conjunctivae became suffused. On day 6 the temperature fell by crisis, and the headache and nausea passed off. For the next 10 days the only symptom was weakness; but on day 16 there was a recurrence of fever, malaise, and nausea which lasted only 24 hours. Apart from weakness the subsequent convalescence was uneventful and the man returned to work on day 28.

Blood cultures, from days 2–5, proved to be positive although on 2 occasions the blood level of chlortetracycline was 1·28 μgm./ml.; but urine cultures were negative (days 5, 7, 11, 13 and 16). Hamsters and guineapigs, inoculated with the patient's blood, developed no evident disease; but the organism was recovered from their blood and kidneys.

The other laboratory findings corresponded with those often encountered in the milder clinical forms of leptospirosis. However, the white blood cell counts are worth noting: day 5—total, 3,500 per cmm., polymorphs 82%, lymphocytes 14%; day 11—total, 6,300 per cmm., polymorphs 47%, lymphocytes 49%. Similar patterns have been reported before.

The authors note that the clinical picture in this patient resembled influenza or *la grippe* and state that it may be caused by leptospirosis more commonly than is generally recognized. *L. H. Turner*

VIRUS INFECTIONS

The order in this section is:—***General, Psittacosis-Lymphogranuloma group, Pox group, Respiratory group, Reovirus group, Enteric group, Arthropod-borne group, Others.***

RIV. ISTITUTO SIEROTERAP. ITAL. 1960, Mar.–Apr., v. 35, No. 2, 153–345, illustrated. [Numerous refs.] Atti del simposio sulle infezioni da virus ECHO e sul morbillo, Napoli 14 Novembre 1959. **[Proceedings of a Symposium on ECHO Virus and Measles Infections, Naples, 14 November, 1959]**

In November 1959 the Italian Institute of Serotherapy held a Symposium in 2 sessions, the second of which, reviewed here, was devoted to infections caused by ECHO viruses. The 6 papers which were presented are something more than the usual contribution to a Symposium, and with their lengthy bibliographies provided with titles and the extensive coverage of their subjects should rather be regarded as monographs. The first paper, by F. MARCOLONGO (*Clinical aspects of diseases caused by ECHO viruses*, pp. 153–242), lists the types of disease caused by the ECHO viruses, and the types of virus which are responsible for them. Each disease is

then considered in detail, with an extensive account of the epidemics which have been reported in the literature, as well as a description of the symptomatology, clinical findings, course and outcome. There are some striking but poorly reproduced photographs of types of exanthem observed in epidemics in Kiel and Osnabrück and elsewhere in Germany in 1958–1959, which were shown to be due to ECHO viruses of types 5, 10 and 12. The paper is provided with 271 references.

The paper of G. Rita (*Epidemiology of ECHO virus infections*, pp. 243–287), is equally detailed, and begins with a review of the distribution of ECHO viruses in the human environment. They are not infrequently isolated from healthy children, particularly of low socio-economic status, but are less commonly encountered in adults. There is also a marked seasonal incidence, the viruses usually being encountered in the summer and autumn, in particular between June and October, and the incidence of infection is considerably higher in tropical and sub-tropical regions. The viruses spread rapidly among closed communities, and the epidemiology of a number of different types is considered in detail, with particular reference to type 20 (JV-1 virus). Infections occur in waves due to a particular type, and the viruses must be considered to be pathogens and not as members of the normal intestinal flora. The paper ends with a bibliography of 161 references.

In the next paper (*The ECHO viruses and their relation to the other enteroviruses*, I. Archetti and A. Felici, pp. 288–303) the 28 types of ECHO virus found up to 1959 are listed, together with their country of origin and the clinical picture of the disease produced by them, and their relationship with poliomyelitis and Coxsackie viruses within the framework of the enteroviruses is discussed.

In *Methods of studying the ECHO viruses* (pp. 304–320) V. Monaci describes the practical aspects of isolating ECHO viruses from various pathological materials as carried out in his laboratory. Trypsinized cultures of cynomolgus or rhesus monkey kidney cells are used, and the strains isolated are identified by neutralization with reference antisera. With some types inhibition of haemagglutination can be used. The relationship between clinical and laboratory findings, antigenic structure and the production of plaques are also discussed.

In the following paper (*The haemagglutination reaction in the ECHO viruses*, pp. 320–324, by L. Dardanoni) the haemagglutination produced by certain types of ECHO virus is compared with that produced by influenza virus; it resembles it in being associated with the virus particle, but differs in that only human red cells are affected, the effect is not abolished by treatment of the red cells with receptor-destroying enzyme or potassium periodate (except in the case of ECHO 10), and cells treated with ECHO virus can still be agglutinated by myxoviruses and *vice versa*. Haemagglutination is only produced by types 3, 6, 7, 10, 11, 12 and 19, and the phenomenon thus enables the ECHO viruses to be classified into 2 subgroups. In the author's experience 104 haemagglutinating strains all belonged to the above types, whereas 79 non-haemagglutinating strains of enterovirus belonged to other types or were poliomyelitis and Coxsackie viruses.

The symposium ends with a brief communication by V. Cilli (*The presence of so-called "Orphan" viruses in Animals*, pp. 325–331), followed by 14 pages of discussion. *D. J. Bauer*

Lippi, M., Frugoni, G. & Benedetto, A. Contributo sieroimmunologico alla conoscenza delle principali virosi. Ricerca nei soggetti sani degli anticorpi devianti il complemento verso il virus dell'ornitosi. **[Complement-Fixing Antibodies Against Ornithosis-Psittacosis Antigens Among Healthy Persons in Rome]** *Arch. Ital. Sci. Med. Trop. e Parassit.* 1960, Nov., v. 41, No. 11, 563–94. [168 refs.]

The English summary appended to the paper is as follows:—

"In the introduction the authors review the virological, clinical and epidemiological data concerning ornithosis-psittacosis, and particularly its spread in Rome.

"The experimental part of the paper concerns the finding of the serum antibodies fixing the complement towards an ornithosis antigen in different groups of healthy individuals i.e.: I) in 407 inhabitants of Rome, of different ages, in 10·0% of whom there was evidence of antibodies; II) in 71 adult individuals belonging to an agricultural community in the Roman Agro, none of whom had a significant ratio of antibodies; III) in 59 children of a Hospital Institution in the province of Rome, in whom 5·1% of positive results were found; IV) in 8 attendants at the Zoo in Rome, 5 of whom had a high ratio of antibodies."

Chervonskii, V. I. **Detection of Complement-Fixing Antibodies in Certain Species of Birds and Mammals in the Complement-Fixation Test with Ornithosis Virus Antigen.** *Problems of Virology.* London. 1960, v. 5, No. 1, 85–9. [10 refs.] [Translated from Russian].

Ornithosis antibodies were found in 44 of 95 Moscow pigeons and 10 of 72 cows slaughtered in the Moscow Meat Combine. *S. P. Bedson*

Seymour-Price, Muriel, Cachia, C. & Fendall, N. R. E. **Smallpox in Kenya.** *East African Med. J.* 1960, Oct., v. 37, No. 10, 670–75.

This is mainly a statistical survey of the incidence of smallpox (variola major and variola minor) in Kenya since the year 1911. Where the mortality rate is not given it is not possible to differentiate between the two varieties of the disease. Peak years were 1916 and 1918 with some 2,600 cases each; 1934—when some 1,600 cases occurred, with a mortality rate of 30%; and 1943 and 1944 with some 3,400 cases each, mainly of variola minor.

In the early years infection was introduced from India, Abyssinia, and Arabia. The route from India through the port of Mombasa has continued to play an important part in this history. Infection in the outbreak of variola

major in 1934 was introduced by nomadic Somalis entering Kenya through the Northern Frontier from Italian territory; and in the much more limited epidemic of 1937 the disease was brought, again *via* the Northern route, by Abyssinian refugees.

Following a decline in prevalence of smallpox amounting almost to complete absence of the disease in 1948 and 1949 in spite of a flow of immigrants from India, some resurgence took place during 1955 and succeeding years —by introduction of variola minor through Northern Province.

Latterly, although there has been a considerable overall decrease in numbers of cases, the highest incidence has been in the Rift Valley Province with Nairobi City showing the next heaviest attack rate, and a low incidence at the Coast and in Central and Nyanza Provinces —an almost complete reversal of the earlier pictures of epidemics.

J. Pickford Marsden

HERRLICH, A. **[The Pox Diseases, Viruses, Epidemiology and Clinical Aspects]**

This book was reviewed on p. 312.

WEARY, P. E., WHEELER, C. E., LINGAMFELTER, C. S., Jr. & CAWLEY, E. P. **Localized Accidental Vaccinia.** *Arch. Dermat.* 1960, Nov., v. 82, No. 5, 804–11, 7 figs. [30 refs.]

3 cases of accidental vaccinia are presented. Lesions on the external genitalia of a girl aged 5 years acquired from a recently vaccinated elder sister (bedmate); 2 lesions on the face of a boy aged 3 years derived from a recently vaccinated sister—a younger sibling, subject of atopic eczema, developed progressive eczema vaccinatum; and a lesion on the left nostril of a girl aged 6 years who bore a deliberate "take" on her left arm.

The true incidence of localized accidental vaccinia is not known. Doubtless infection is commonly spread by fingers [though lesions actually on digits are rare, except in the case of laboratory and allied workers with the virus] but inanimate objects—clothing, handkerchiefs, towels, etc., may play an important part.

Diagnosis may be difficult unless the possibility of the condition is kept in mind. Perhaps the most helpful features are known susceptibility of the subject and proximity to a deliberate vaccinia lesion on himself or another member of the family.

Lesions on mucous membranes may present a confusing picture: on the eye, especially if the cornea becomes involved, they may be most serious. Otherwise symptomatic treatment usually suffices and the need for cortisone [which may be contra-indicated] or hyperimmune gamma globulin should seldom arise.

J. Pickford Marsden

DOLL, R., HILL, A. B. & SAKULA, J. **Asian Influenza in Pregnancy and Congenital Defects.** *Brit. J. Preventive & Social Med.* 1960, Oct., v. 14, No. 4, 167–72. [11 refs.]

In a prospective investigation of 175 women who had suffered an attack of Asian influenza before, during, or after their pregnancy (128 verified as far as possible), observations were made on the 177 infants born subsequently. No hazard to the foetus was detected in those cases in which the illness fell within the pregnancy (88 cases), or, in particular, in its early stages. These negative findings are in contrast to those reported in some other studies [this *Bulletin*, 1960, v. 35, 271], and particularly to the increase in the stillbirth rate due to anencephaly reported in Scotland in 1958, and to a lesser extent in 1959.

It is provisionally concluded that infection of the mother with Asian influenza during the early months of pregnancy probably increases the risks of anencephaly, but that the extent of the hazard is normally small.

H. Stanley Banks

BROUN, G. O., OLIGSCHLAEGER, D., LEGIER, M. & SCHMIDT, R. R. **Studies of the Epidemiology of Influenza as demonstrated by Serum Pools. II. Evidence of Inapparent Influenza Infections and General Level of Population Resistance as shown by the Antihemagglutinin Reaction in Serum Pools collected by Random Sampling.** *Arch. Intern. Med.* 1960, Oct., v. 106, No. 4, 496–512, 7 charts. [24 refs.]

Serum pools collected between July 1948 and June 1959 in the St. Louis area were used in haemagglutination-inhibition tests. More than 90% of the sera were from adults. Before 1952 the pools comprised relatively few sera but between 1952 and 1956 they averaged 740 sera per week which represented about a 1% sample of the population under study. The sera were treated with RDE or periodate and assembled in weekly, monthly or quarterly pools.

Epidemics of influenza B in 1952 and influenza A in 1953 were reflected in increases of antihaemagglutinin in serum pools from 0 to over 1/25 and from 1/5 to 1/80, respectively. The homologous antibody rise was usually at least 4 times the pre-epidemic level. Following epidemics caused by influenza A viruses there were also increases in antibody against other influenza virus strains which were not prevalent at the time; this was noted, for example, with strain A-Swine-1931 which had not been isolated since 1935. Occasionally, heterologous antibody rises were so marked that the strain responsible for the outbreak could not be recognized by the height of the antibody rise.

The Asian influenza pandemic was first recognized in the St. Louis area in September 1957, but several pools collected in 1948–49, 1950 and 1951 showed high titres against the A2-St. Louis and A2-Japan-305-1957 strains [a surprising finding, particularly with pooled sera]; this suggested an antigenic relationship between these strains and a virus prevalent in 1948–51.

Finally, there was a rise in antihaemagglutinins to Sendai-1952 virus in 1949–50, 1955 and 1957–58; this suggested exposure to the virus although there were no clinical outbreaks [there have not, so far, been any reported isolations of this virus in America]. In preliminary work with haemadsorption virus 2 (HA2) the authors were not able to duplicate the pattern of haemagglutinins shown by Sendai virus.

D. Taylor-Robinson

HIMMELWEIT, F. **Serological Responses and Clinical Reactions to Influenza Virus Vaccines.** *Brit. Med. J.* 1960, Dec. 10, 1690–94, 5 figs. [11 refs.]

In the first set of trials A/England/211/56 virus purified by ultracentrifugation and inactivated with formalin was emulsified with Drakaol No. 6 and purified Arlacel A in a machine which, by mechanical adjustment, gave vaccines of various viscosities; namely high (treacly), medium, and low (like fairly light mineral oil). Each type contained 2,000 HA units per dose. In the second set of trials vaccines were prepared from purified A/Singapore/1/57 and contained from 2·5 mgm. to 10 mgm. of aluminium phosphate per dose and 20,000 HA units of virus. In each case control vaccines were prepared in which the virus was suspended in saline. 253 volunteers took part in the first trial and 400 in the second and the results were assessed by clinical observation and by haemagglutination-inhibition tests on serial blood specimens.

It was concluded that the antibody responses to the emulsified vaccine were much better than those to the saline vaccine and there were no local or general reactions with emulsified vaccines and a few with saline vaccines. There was no decrease in the activity of emulsified vaccines stored for 1 month at 4°C. On the other hand aluminium phosphate had no adjuvant effect and did not reduce the reaction rate. It is pointed out that previous studies showed that aluminium phosphate reduced the reaction rate to vaccines but that this might have occurred because the vaccines were prepared from unpurified virus and therefore the addition of aluminium phosphate during manufacture eliminated many impurities from the final product. *D. A. J. Tyrrell*

HENEBERG, D. & GERBEC, M. **The Significance of High Complement-Fixing Antibody Titres in the Serological Diagnosis of Influenza A.** *J. Hyg. Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 2, 182–90, 3 graphs.

Cases of influenza occurring in a military camp in Yugoslavia during the 1957 Asian influenza epidemic were studied. The geometric mean complement-fixing (CF) antibody titre of sera from uncomplicated cases was 1:44 and that for cases with severe pulmonary complications was 1:1044. The authors, therefore, analysed routine serological data for influenza A infections from April 1955 to September 1958 and correlated this information with clinical notes that were submitted with each blood sample. On the basis of this clinical information, cases were grouped as "pneumonic" (1,730 sera tested) or "non-pneumonic" (1,063 sera tested). Sera with a titre greater than 1:128 occurred relatively more frequently in the pneumonic group than in the non-pneumonic group. The authors concluded that CF antibody titres above 1:128 suggested with increasing probability influenzal pneumonia, but hastened to add that this did not hold for an individual case.

D. Taylor-Robinson

NAKAO, T. **A Fatal Case of Meningoencephalitis due to Hemagglutinating Virus of Japan.** *Tohoku J. Exper. Med.* 1960, Sept. 25, v. 72, No. 2, 197–200.

"A fatal case of aseptic meningitis caused by HVJ was reported. From cerebrospinal fluid and blood of the patient HVJ was isolated. Though the prognosis of aseptic meningitis caused by HVJ is generally good, it should be borne in mind that a child seriously ill with some damage or other in the brain as the present case may die of virus meningitis."

BELL, T. M., TURNER, Grace, MACDONALD, A. & HAMILTON, D. A. **Type-3 Adenovirus Infection.** *Lancet.* 1960, Dec. 17, 1327–9, 1 fig.

32 out of 95 boys living in a closed community in a rural area of Scotland developed a febrile illness (temperature 99–104°F.) with upper respiratory tract signs and some stiffness of the neck and back and some gastro-intestinal symptoms. Only 2 showed conjunctivitis.

Faeces were collected from 11 patients and adenovirus type 3 was isolated from 10, (and also from 4 of 5 throat swabs and 1 conjunctival swab from the same 11 patients). Rising titres of antibody against type 3 adenovirus were detected by complement-fixation and neutralization tests on paired sera from 7 patients. The authors compared the efficiency of different tissue cultures for detecting viruses in faecal emulsions. Virus was detected in all 10 specimens with the 4 cell types used but the time required for degeneration to occur varied —with HeLa cells it averaged 9·6 days, with human amnion 9·7, human embryonic kidney 5·3 and human embryonic liver 3·6 days. They conclude that their patients were infected with adenovirus type 3 but point out the difficulties in proving that the virus caused the disease although it almost certainly did.

D. A. J. Tyrrell

DAWSON, C., JAWETZ, E., HANNA, L., WINN, W. E. T. & THOMPSON, C. **A Family Outbreak of Adenovirus 8 Infection (Epidemic Keratoconjunctivitis).** *Amer. J. Hyg.* 1960, Nov., v. 72, No. 3, 279–83. [11 refs.]

In the autumn of 1959 a lorry driver, his wife, two small girls and infant son developed in turn illnesses of varying severity in which conjunctivitis was part of the clinical picture. One child had a cold and sore throat in addition. 2 baby-sitters who had cared for the children about the time they started to be ill developed severe follicular conjunctivitis themselves. The typical opacities of epidemic keratoconjunctivitis (EKC) were seen in the wife and 2 baby-sitters. Adenovirus type 8 was isolated from one baby-sitter and one daughter and both showed a rising titre of neutralizing antibody against the virus. Neutralizing antibodies were present in sera collected from both parents several weeks after the onset of the disease. The disease did not spread to further contacts of the patients described. The authors believe this is the first such family outbreak of type 8 adenovirus infection in North America or Britain, though it is

common in Japan as also is the atypical and relatively infectious "infantile EKC" seen in the young children of this family. *D. A. J. Tyrrell*

LAURINSICH, A., BASSANETTI, F. & GIOVANNELLI, G. La clinica delle adenovirosi. [**Clinical Aspects of the Adenovirus Infections**] *Giorn. di Malattie Infettive e Parassit.* 1960, Nov., v. 12, No. 11, 857–945, 23 figs., 1 diagram & 2 graphs. [Numerous refs.]

This paper, which was presented to the XI National Congress of the Italian Society for the Study of Infectious and Parasitic Diseases held at Palermo in December 1960, is so long and detailed (it takes up 83 pages of close print and there are no less than 216 references) that it really constitutes a monograph; an abstract cannot therefore do it justice since only certain points can be mentioned.

The paper is based on the examination of 507 children aged between 30 days and 13 years who for the most part were patients in the Paediatric Clinic of the University of Parma, the great majority of the remainder being healthy children in the Parma Provincial Orphanage, and, contrary to what might be imagined from the title, is really divided into two parts, I dealing with virological and serological investigations, II with clinical aspects.

I. Of the 507 children attempts were made to isolate the virus in all, complement-fixing antibodies were estimated in 307, and neutralizing antibodies in 39. In the 2 latter, samples of serum were taken in both the acute and convalescent phases, only those being regarded as positive where the second specimen showed a 4-fold rise in titre over the level in the acute stage. Swabs were taken from the pharynx, faeces and sometimes from the conjunctiva. Virus was isolated in 68 cases, usually within the first 10 days, but in 1 case at least was isolated from the faeces 25 days after. Type 7 adenovirus was by far the most frequently isolated, then types 3, 5, and 2 in that order; several strains had not been typed when the paper was published. In addition animal experiments were carried out on 10 adult rats with type 3 as that was found to be most closely associated with a definite pharyngeal infection; in some instances to render them more receptive the rats were pre-treated with cortisone. No virus was recovered from any of the animals.

II. Out of the whole 507 children, only 68 were considered positive and were then divided into 3 groups: (1) definite adenovirus infection, 41; (2) probable, 7; (3) possible, 20. Clinical details often with extensive laboratory investigations are given for each of the 68 cases, sometimes an ECG, or an EEG tracing was made. In several patients the infection occurred in hospital, among these being patients suffering from acute glomerulo-nephritis, staphylococcal pneumonia, and meningococcal meningitis. Apart from fever which was invariable, the usual symptoms were headache, vomiting, constipation, diarrhoea; on examination there was reddening of the pharynx, and enlargement of the lymph glands, usually the posterior cervical but sometimes more extensive or even generalized; infections of the lungs and bronchi occurred frequently. No patient died, 1 patient had an acute myocardial condition which had not resolved entirely on discharge, here no adenovirus was isolated but complement-fixing antibodies were found in the 2nd specimen of serum at titres of 1 in 64 or more, and antibodies against other respiratory viruses were not found. In 3 there was some evidence of an encephalitic condition as shown by the EEG in which the normal alpha-rhythm disappeared and was replaced by larger slower waves often of delta type; these disappeared and the normal waves returned on the patient's recovery.

Treatment was symptomatic and antibiotics were useless. For prevention the authors suggest that a vaccine made from the most common types, *i.e.* 7, 3, and 5, may be helpful, and they tested this on 24 children. An increase in neutralizing antibodies was found which was especially marked after a booster dose 30 days later.

Finally they discuss the very difficult problem of latency.

[The authors have produced an imposing mass of evidence, and their reports on the 68 clinical cases are well worth study. The case of the patient with possible viral myocarditis recalls an analogous condition in horses.] *W. K. Dunscombe*

JACKSON, G. G., DOWLING, H. F., ANDERSON, T. O., RIFF, Louise, SAPORTA, J. & TURCK, M. **Susceptibility and Immunity to Common Upper Respiratory Viral Infections—the Common Cold.** *Ann. Intern. Med.* 1960, Oct., v. 53, No. 4, 719–38, 11 figs. [32 refs.]

This paper summarizes nearly 8 years' experimental work at the University of Illinois College of Medicine. Much of it has been published previously but some new data are given. The authors have worked mainly with nasal secretions from which they could not isolate viruses in laboratory tests and point out that these represent the commonest type of agent causing colds in man. These secretions were shown to cause colds by administering them as nasal drops to volunteers (who were not isolated). Other volunteers had non-infectious inocula at the same time. The volunteers were observed by a clinical observer who was uninformed as to the nature of the material given each volunteer and the results were evaluated by comparing the symptoms and signs in the inoculated and control volunteers. The secretions produced a spectrum of illnesses, the most common of which was the common cold. Several secretions produced identical clinical effects; 3 secretions produced in 3, 19 and 38% of volunteers respectively a syndrome of sore throat, hoarseness and cough, and the incubation periods also differed; these viruses could thus be distinguished on clinical grounds. Secretions no longer produced colds after incubation with pooled human gamma globulin, and volunteers who had had a cold after inoculation with a particular nasal secretion were immune on reinoculation with that secretion and not with another. The authors conclude that the secretions they used contained antigenically different viruses which elicited a specific immune response. During experimental colds, scrapings of nasal epithelium were taken. These were examined by Papanicolou's method. Specimens from 4 subjects without colds contained about 40% of abnormal

cells; in 8 volunteers who developed colds this figure rose to over 70% two days after inoculation.

The factors affecting susceptibility to colds were also examined. Volunteers gave history of having on the average different numbers of colds each year. When non-infectious materials were given, those volunteers who reported they had frequent natural colds were more likely to develop colds than were those who reported infrequent natural colds. There was no such difference in the number of colds following the inoculation of infectious material. The report of symptoms seemed to be influenced by psychological make up. Chilling for 2 hours did not influence the frequency of colds. Women inoculated during menstruation had fewer colds than expected and those inoculated in the preovulatory or premenstrual phase had more colds than expected—these findings could not be satisfactorily correlated with any physiological or humoral changes.

[This paper is well worth reading in the original, though the reviewer would have liked to have been given more details of some of the previously unpublished work.] *D. A. J. Tyrrell*

McNAMARA, M. J., THOMAS, Eleanor H., STROBL, Annette & KILBOURNE, E. D. **Minor Disease in Ten "Healthy" Adults. An Intensive, Day-by-Day, Clinical and Virologic Study.** *Amer. Rev. Respiratory Dis.* 1960, Oct., v. 82, No. 4, 469–81, 6 figs. [25 refs.]

5 men and 5 women, all associated with the laboratory in which the study was carried out, were assessed by clinical observations and by virological methods from September 1958 to May 1959. One person recorded the symptoms of each subject, daily; a symptom was considered to be any departure from physical well-being. Pharyngeal swabs were obtained from each person 3 times per week and inoculated immediately into HeLa cells or into secondary monkey kidney cultures or frozen to −70°C. prior to inoculation.

The average number of symptom-free days per person was 120 of the 266 total days (45%). Slightly less than 50% of all symptoms involved the respiratory tract and 6% the gastrointestinal tract. 2 to 10 "colds" occurred per person during the 9-month period. Although on the average each subject was symptom-free for less than half of the period of the study, he was away from work for only 1·5 days altogether. Of the total of 15 days lost from work, 11 were due to respiratory symptoms and 4 to gastrointestinal symptoms. No cytopathic agents were isolated from a total of 439 throat and 11 rectal swabs and in only 2 instances was there serological evidence of infection—influenza B in one case and an adenovirus in another. The authors conclude that minor disease was greater than expected, aetiologically undefinable and that absenteeism was a poor guide to its incidence.

[It would be interesting to repeat these studies with the techniques used to isolate viruses from persons with common colds [TYRRELL *et al.*, this *Bulletin*, 1960, v. 35, 616].] *D. Taylor-Robinson*

WELLS, A. V. **Antibodies to Poliomyelitis Viruses in St. Lucia.** *West Indian Med. J.* 1959, Sept., v. 8, No. 3, 161–70, 1 fig.

A survey of poliomyelitis virus antibodies was made among the poorer classes of the population of the island of St. Lucia in the Caribbean. 227 sera were studied and all but 1 contained antibodies to 1 or more types of poliomyelitis virus. 87% were positive to all 3 types of virus. Under the age of 5 years 67·5% of the sera contained antibodies to all 3 types of virus. The titres of antibody were relatively low, only 11% being 1 in 20 or more. Paralytic poliomyelitis is a rare disease on the island. Only 14 cases have been notified in the years 1949–58 in a population of about 91,000. The author concludes that poliomyelitis virus infection occurs early in life under the cover of maternal antibodies which prevent clinically manifest infection. *A. J. Beale*

NIEDERMAN, J. C., HORSTMANN, Dorothy M. & OPTON, E. M. **A Survey of Poliovirus Antibody Levels in New Haven, Connecticut, 1957–1958.** *Amer. J. Hyg.* 1960, Sept., v. 72, No. 2, 218–30, 7 figs. [20 refs.]

A 2-year study was made of poliomyelitis virus neutralizing and complement-fixing antigens in low and high socio-economic groups in New Haven in 1957 and 1958. The analysis is based on persons 5–49 years old. In unvaccinated persons, as has been noted before, neutralizing antibodies are acquired later in the higher than in the lower socio-economic groups, but over the age of 20 both groups are very similar. Complement-fixing antibodies are present only in a low percentage. In vaccinated persons (3 doses) the differences between socio-economic groups were not noted, both groups having high levels of antibody at all ages and both having higher titres and incidence of antibodies than the unvaccinated lower socio-economic group. Complement-fixing antibodies were present in many more vaccinated people, not only aged 5–9 but also 15–19, when peak incidence was often noted. One year later there was no decline of antibody level in unvaccinated persons (natural immunes) but a slight decline in vaccinated subjects for types 1 and 3. Thus 3% and 9% of the people with antibodies to types 1 and 3 lost them after 1 year.

In 1959 there was a sharp outbreak of poliomyelitis in New Haven, concentrated among the young (under 5) children and lower socio-economic group. There were 13 paralytic cases among people over 5, 3 of whom had had 3 doses of vaccine. There were 26 paralytic cases in children of 0–4 years, and 8 had had 3 or more doses. However, all but 11 had had at least 1 dose of vaccine. Unfortunately, in the serological study, too few children under 5 were studied, but in 1957 20 vaccinated children were studied. 65% had type 1, 85% type 2 and 60% type 3 antibodies. The authors estimate that this is 10–15% less for types 1 and 3 than was found in older children given vaccine. This relatively poorer response of young children doubtless explains the numbers of vaccinated infants developing poliomyelitis

A. J. Beale

REINHARD, K. R.; GIBSON, H. V.; GERLOFF, R. K.; PHILIP, R. N. **Immunity towards Poliovirus among Alaskan Natives. I. Comparative Reported Incidence of Clinical Poliomyelitis in Alaskan Natives and Non-Native Residents, 1950–1954** [REINHARD & GIBSON]. *Amer. J. Hyg.* 1960, Nov., v. 72, No. 3, 289–97. [12 refs.] **II. A Serologic Survey of 47 Native Communities of Western and Northern Alaska** [REINHARD & GERLOFF]. *Ibid.*, 298–307, 1 fig. [11 refs.] **III. A. Study of Naturally and Artificially Acquired Antibodies against Poliovirus among Residents of Two Bering Sea Communities** [REINHARD, GERLOFF & PHILIP.] *Ibid.*, 308–20, 4 figs. [16 refs.]

These 3 papers present an interesting study of the epidemiology of poliomyelitis in natives of Alaska. Since the observations of serious, explosive outbreaks of poliomyelitis and the finding of a low incidence of specific antibodies in Eskimo populations, it has become accepted that these populations represent virgin soil for poliomyelitis virus. In the first paper the authors show that the incidence of poliomyelitis in the years 1950–54 in Alaska has been lower in the native population, especially in those in the villages.

In the second paper the explanation is found in the high incidence of antibodies among natives of Alaska aged between 17 and 52. Less than 1% had no antibodies to any type of poliomyelitis virus. Type 2 antibodies were most prevalent and type 3 least prevalent. The results varied in different geographical localities. Sera from 3 areas had been examined 5 years and 1 year earlier by PAUL *et al.* [*J. Immunology,* 1951, v. 66, 695; this *Bulletin,* 1951, v. 26, (1047); 1952, v. 27, 290] and EKLUND and LARSON [*ibid.*, 1956, v. 31, 800] respectively. The new results show that poliomyelitis virus infections were more prevalent in 1955 than the earlier results implied. Types 1 and 2 antibodies were found to be very prevalent in the areas previously studied by Paul *et al.* contrary to expectations. The new results agree that type 3 antibodies were only present in individuals over 36 years. In St. Paul village, in addition to prevalent type 3 antibodies observed by Eklund and Larson, type 2 antibodies were also prevalent 1 year later.

In the third paper an antibody survey is described which was made in 1955 and 1957 in St. Lawrence Island in the Bering Sea. The acquisition of antibodies by age was studied although few pre-school children were sampled. Antibodies to all 3 types were prevalent but the age of maximal incidence varied. For type 1, antibodies were rare in the 6–10-year age-groups and reached a peak of nearly 70% between 16–20. Type 2 antibody incidence was already at its peak between 6–10 years and then fell slightly to rise again over 40 years of age. Type 3 followed a similar pattern to type 1. Some of the individuals had been vaccinated and these had much higher incidence and titres of antibodies. *A. J. Beale*

AULD, P. A. M., KEVY, S. V. & ELEY, R. C. **Poliomyelitis in Children. Experience with 956 Cases in the 1955 Massachusetts Epidemic.** *New England J. of Med.* 1960, Dec. 1, v. 263, No. 22, 1093–100, 1 fig. [18 refs.]

This is an analysis of 956 cases of poliomyelitis occurring in children under 16 years of age in Massachusetts in 1955. There are numerous tables referring to age and sex distribution, site of paralysis and the like, but there is nothing new in the article. The authors feel that because of the possible reduction to a bare minimum of paralytic poliomyelitis as a result of immunization it is pertinent to record details of this epidemic. *A. B. Christie*

YOUNG, D. G. & SPROULE, B. J. **Paralytic Poliomyelitis at the University of Alberta Hospital.** *Canadian Med. Ass. J.* 1960, Nov. 26, v. 83, No. 22, 1140–43, 2 figs.

This is an account of 55 cases of paralytic poliomyelitis treated at the University of Alberta Hospital in the year 1957–59: type 1 poliovirus was isolated in 29 out of 50 cases studied. Coxsackie virus A9 was isolated from the stool of one paralytic case but serum titrations were negative. Of 33 paralytic patients treated in 1959, 8 had had 3 injections of Salk vaccine, but it is not apparent from the article whether virus was isolated from these vaccinated patients. An addendum states that from 1st January to 1st November 1960, 78 patients with paralytic poliomyelitis had been admitted, of whom 38 (48·7%) had received 3 or more injections of Salk vaccine.

[The most interesting part of this article concerns vaccination failures and it is unfortunate that fuller information regarding virus culture in these failures is not given.] *A. B. Christie*

THIODET, J., MASSONNAT, J. & FOURRIER, A. Note sur la fréquence et l'épidémiologie de la poliomyélite en Algérie. A propos de 686 cas observés en quatre ans à la clinique des Maladies Infectieuses, hôpital d'El-Kettar. **[Incidence and Epidemiology of Poliomyelitis in Algeria. Observations on 686 Cases seen in 4 years in the Infectious Diseases Clinic of El-Kettar Hospital]** *Bull. Acad. Nat. Méd.* 1960, v. 144, Nos. 29/30, 704–8.

The 4 large, recent outbreaks of poliomyelitis in Algeria have been mainly confined to infants and young children. During the 4 years 1956–59 poliomyelitis accounted for 11·2% of all infectious diseases among children under 12 years of age admitted to the infectious diseases hospital but only 0·6% of the infectious diseases among adolescents and adults. 603 of the 686 cases were in children under 5 years of age and of these two-thirds were aged between 6 months and 2 years. 25 of the 33 adults attacked were members of the services from France. The sex ratio of poliomyelitis was 420 males to 266 females. Respiratory complications were present in 72 patients (48 children, 2 adolescents and 22 adults). The mortality for the respiratory form was 34·7%. Lumbar puncture was carried out in 36 cases after paralysis had appeared, in 19 there was no apparent effect but in 18 a worsening of the paralysis or of the respiratory symptoms occurred. Although it cannot be asserted that this was cause and effect, the authors remark that the coincidence was disturbing. *W. J. Martin*

Lo Monaco, G. B. & Cremoncini, R. Osservazioni sulla eliminazione di virus in malati di poliomielite. **[Observations on the Excretion of Virus in Patients Suffering from Poliomyelitis]** *Giorn. di Malattie Infettive e Parassit.* 1960, Mar.–Apr., v. 12, Nos. 3/4, 161–8, 1 fig. [Numerous refs.]

The authors have investigated the duration of excretion of poliomyelitis virus in 95 children aged up to 13 years admitted to hospital in Florence with paralytic poliomyelitis in 1957–59. Type 1 virus was isolated from the faeces in 61 (64%), type 2 in 6 (6%), type 3 in 12 (13%), and other cytopathogenic agents in 3 (3%) instances. Poliomyelitis virus was no longer excreted after 3 weeks in 24 of 43 (56%) patients who were studied for an adequate period, and excretion ceased after 4 weeks in 16 (38%) patients. No virus could be recovered 11 weeks after the onset of illness. During the investigations 9 instances of asymptomatic hospital infection with another type of poliomyelitis virus or with an unidentified cytopathogenic virus were observed. *D. J. Bauer*

Belian, W., Rademacher, I. & Käppel, M. Neutralisierende Antikörper und isolierter Poliomyelitis-Virus-Typ. **[Neutralizing Antibodies and Poliovirus Type Isolated]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 4, 457–60.

The English summary appended to the paper is as follows:—

"In 90 per cent of 7,500 tests the poliovirus type isolated and the type of neutralizing antibodies found in the blood of the same patient corresponded.

"For the examination it is recommended to take a stool and a blood specimen, as early as possible during the course of the disease, and, moreover, a second blood specimen during the third or fourth week of illness. Both sera should be examined together. The chance of isolating virus is the best from stool specimens and the poorest from cerebro-spinal fluids."

Kendall, E. J. C., Vollum, R. L., Beswick, T. S. L., Miller, Ann & Tobin, J. O'H. **The Antigenic Activity of some Poliomyelitis Vaccines used in the United Kingdom in 1958.** *J. Hygiene.* 1960, Dec., v. 58, No. 4, 399–408. [16 refs.]

This interesting paper compares the response of 172 public school boys and 14 young medical personnel, all of whom lacked poliomyelitis virus antibodies, to 9 poliomyelitis vaccine preparations. The response in human beings was compared with that in monkeys. The authors conclude from earlier studies [Kendall *et al.*, and Logan *et al.*, this *Bulletin*, 1960, v. 34, 1017] that a satisfactory killed poliomyelitis vaccine should induce a titre of at least 1 in 100 after the booster dose by their methods of testing. They calculate from the rate of decline of antibodies that such vaccines would give a protective effect for at least 5 years. If the vaccines are insufficiently potent to achieve these levels a 4th dose 1 year after the 3rd would almost certainly achieve these titres. The results show that for types 2 and 3 all the vaccines produced reasonably good responses. 3 and 8 people failed to achieve titres of 1 in 100 after a booster dose to types 2 and 3 respectively. The response to type 1 was, however, less good. Only 1 vaccine gave 100% of titres higher than 1 in 100. This was an experimental vaccine consisting of 1 ml. of a routine batch (vaccine H) of commercial poliomyelitis vaccine to which was added an extra 1 ml. of a type 1 inactivated monovalent component. Between 40 and 80% of the individuals responded with titres of 1 in 100 to a booster dose (some subjects had 3 primary doses if the titre after 2 doses was less than 1 in 4). 40 schoolboys with antibodies to type 2 but not to types 1 or 3 were also tested. These boys responded better to type 1 than people without type 2 antibodies. Their response to type 3 was not affected.

The results of comparisons between monkey potency and response in man were erratic. The monkey potency test as at present performed is not considered adequate. The authors advocate the use of one of the vaccines tested (vaccine H) as a standard for the potency test for killed poliomyelitis vaccine. They also consider that a more accurate potency test employing more than 12 animals should be used to standardize vaccine.

[3 conclusions seem to emerge from this paper. First, the potency of the type 1 component of killed poliomyelitis vaccine should be strengthened. Second, a more accurate method of measuring and standardizing potency is required. Third, with vaccines at present in use a fourth dose is required.] *A. J. Beale*

Bordt, D. E., Whalen, J. W., Boyer, P. A., Pursell, A. R. & Staffieri, F. P. **Poliomyelitis Component in Quadruple Antigen. Controlled Clinical Study of Enhanced Response of Children.** *J. Amer. Med. Ass.* 1960, Oct. 29, v. 174, No. 9, 1166–9, 2 figs.

The immunizing ability of a vaccine containing poliomyelitis and pertussis vaccines and diphtheria and tetanus toxoids with aluminium phosphate adjuvant (Compligen, Pitman Moore and Co.) was compared with the performance of poliomyelitis vaccine alone and triple antigen alone. In all, 192 children up to 6 years old were studied. Each child was bled before the vaccination course which consisted of 3 doses at approximately monthly intervals and then bled again 1 month later. It was found that the response of children to poliomyelitis vaccine was better if it was in the combined antigen. Thus, for children aged 6 months to 2 years without antibodies to any type before vaccination, the conversion rate and geometric mean titres were for quadruple vaccine: type 1, 92%, 1/67; type 2, 96%, 1/193; type 3, 92%, 1/45; and for plain poliomyelitis vaccine: type 1, 46%, 1/3; type 2, 82%; 140, type 3, 82%, 1/12. The response to the other components of the quadruple vaccine was good but differed insignificantly from that to triple antigen. [Unfortunately, rather few children under 6 months were studied, since in this age-group the response to antigens, particularly poliomyelitis vaccine, is inhibited by maternal antibody. It may be that vaccine with aluminium phosphate adjuvant is capable of overcoming this inhibition but the study does not shed any light on this.] *A. J. Beale*

RANNON, Lotte, GOLDBLUM, N., SKALSKA, Paula & GOTLIEB, A. **Antibody Response of Newborns to Formalinized Poliomyelitis Vaccine (Salk Type).** *Amer. J. Hyg.* 1960, Sept., v. 72, No. 2, 244–9, 3 figs. [16 refs.]

2 groups of children were given poliomyelitis vaccine in the first 3 days of life. The first group had 2 primary doses 1 month apart with a booster dose between 4 and 6 months of age. The second group had 3 primary doses, the third 2 weeks after the second, and the booster dose. The antibody response assessed after the booster dose showed that while 70% responded for types 1 and 2 and 56% for type 3 in those given 3 primary doses, only 24%, 36% and 45% responded to types 1, 2 and 3, respectively, in infants given 2 primary doses. The antibody titres were also higher in general in children given 3 primary doses. The authors stress that a good response in young children depends upon a potent antigen being used. *A. J. Beale*

RAMON, G. Vaccination contre la poliomyélite et vaccination antidiphtérique. Résultats respectifs. Étude comparative. Conclusion. [**Comparative Study between Poliomyelitis Vaccination and Diphtheria Vaccination**] *Rev. d'Immunologie.* 1960, July–Sept., v. 24, No. 4, 469–95. [Refs. in footnotes.]

Ramon presents a long study of the performance of killed poliomyelitis vaccine in preventing poliomyelitis. He believes that this performance is far from impressive and shows comparisons with the excellent performance of diphtheria prophylactics to bear this out. There is also a review of the development of living attenuated poliomyelitis vaccines but these are considered to be still in the experimental stage. *A. J. Beale*

KLEE, A. **Neurological Complications after Vaccination against Poliomyelitis. Report of a Case of Meningo-Encephalomyelitis.** *Danish Med. Bull.* 1960, Oct., v. 7, No. 5, 142–4.

A case of meningo-encephalitis following upon the fourth dose of killed poliomyelitis vaccine is described. The patient was a 31-year-old female hospital laboratory technician. The site of inoculation of the vaccine is not recorded but within a few hours she felt unwell and developed a headache. She later developed neck stiffness, fever, double vision, vertigo, clouding of consciousness, difficulty in walking, weakness and ataxia, particularly in the left leg which felt as if it were "treading in snow". The inoculation took place on June 6th, 1959 and by October she was sufficiently improved to return to work but in early December she caught a cold and was confined to bed for several days with a raised temperature. Thereafter the headache became worse with double vision, nausea, vomiting and rotatory vertigo. It was suspected that she might have a cerebellar tumour but no evidence for this could be found. Her condition gradually improved so that by February 1960 she could be transferred to a rehabilitation centre. The authors consider that this was undoubtedly a case of a neurological complication of poliomyelitis vaccination, and refer to the extensive reviews of the subject of post-inoculation neurological complications that have been made by MILLER and STANTON [this *Bulletin*, 1954, v. 29, 912] and DE VRIES (*Postvaccinial Perivenous Encephalitis*, Amsterdam, 1960). *A. J. Beale*

ALSOP, J., FLEWETT, T. H. & FOSTER, J. R. **"Hand-Foot-Mouth Disease" in Birmingham in 1959.** *Brit. Med. J.* 1960, Dec. 10, 1708–11, 3 figs.

An epidemic of "hand-foot-and-mouth disease" which took place in Birmingham in 1959 is described. The main clinical features were shallow ulcers in the mouth and a vesicular rash mainly on the hands and feet but occasionally also on the buttocks. Coxsackie A16 was isolated in suckling mice from all of 5 patients examined who had the typical mouth lesions or vesicular rash. The virus was not isolated by inoculation of tissue cultures of human embryo liver cells, embryo rabbit kidney cells, human amnion or the untransformed MK1 line of WESTWOOD *et al.* [this *Bulletin*, 1957, v. 32, 815]. The epidemic seemed very similar to one described by ROBINSON *et al.* (*Canad. Med. Ass. J.*, 1958, v. 79, 615) from which Coxsackie A16 was also isolated. The Canadian A16 virus, however, produced cytopathic changes in tissue cultures and, moreover, showed minor antigenic differences from the prototype Coxsackie A16 strain which were not shown by the Birmingham viruses. *A. J. Beale*

YAFFEE, H. S. **Erythema Multiforme caused by Coxsackie B5. A Possible Association with Epidemic Pustular Stomatitis of Children.** *Arch. Dermat.* 1960, Nov., v. 82, No. 5, 737–9, 1 fig.

The authors refer to an outbreak of stomatitis in children in the summer of 1959: pustular lesions were seen on the anterior half of the buccal cavity and on the lip but not on the tongue. During the same period 4 adults were seen with rashes resembling erythema multiforme. Coxsackie virus B5 was isolated from the throat washings of one of the adults and from throat washings and stools of his son who had been ill 2 weeks previously. The title of the article suggests that the 2 conditions may have been associated and that Coxsackie virus may have been the cause. *A. B. Christie*

LERNER, A. M., KLEIN, J. O. & FINLAND, M., with the technical assistance of Priscilla BILLS. **Infection with Coxsackie Virus Group B, Type 3, with Vesicular Eruption—Report of Two Cases.** *New England J. of Med.* 1960, Dec. 22, v. 263, No. 25, 1305.

"Two infants under one year of age who had a fine, vesicular eruption and from whom Coxsackie virus Group B, Type 3, was isolated are described. Polio-virus Type 3 was also isolated from 1, and concomitant rises in titre of antibody to both viruses were demonstrated in that child."

LEPOW, Martha L., CARVER, D. H. & ROBBINS, F. C. **Clinical and Epidemiologic Observations on Enterovirus Infection in a Circumscribed Community during an Epidemic of ECHO 9 Infection.** *Pediatrics.* Springfield, Ill. 1960, July, v. 26, No. 1, 12–26, 3 figs. [54 refs.]

This is an account of an outbreak of enterovirus infections in a new housing estate of 20 buildings in Milwaukee, each housing 16 families. The study continued over 5 weeks and was concentrated on 8 of the buildings some of which were not affected: 95 people were ill and virus isolation studies were carried out in 288. ECHO virus type 9 was isolated in 34, type 1 in 2, and Coxsackie virus B5 in 28, B4 in 9 and B3 in 1: infection with more than 1 virus was rare. ECHO virus infection caused febrile illnesses associated with a rash in young children and with meningeal irritation in older children and in adults: Coxsackie virus infection did not cause a rash but the illness was otherwise very similar. Inapparent infection with ECHO virus occurred in 17% of persons investigated, with Coxsackie virus in 41%. [This article gives an unusually clear-cut picture of the spread of the enteroviruses.] *A. B. Christie*

KLEIN, J. O., LERNER, A. M. & FINLAND, M. **Acute Gastroenteritis associated with ECHO Virus, Type 11.** *Amer. J. Med. Sci.* 1960, Dec., v. 240, No. 6, 749–53. [17 refs.]

3 adult laboratory workers were taken ill with vomiting, chillness, abdominal cramp and diarrhoea. The acute symptoms subsided within 24 hours and patients were thereafter well. ECHO virus type 11 was isolated from rectal swabs and from serum taken in the acute stage of 2 of the patients. The serum of the third showed a 4-fold rise in antibody titres to ECHO virus type 11.
A. B. Christie

MATHUR, K. S., CHAKRAVARTI, M. G. & AGARWAL, K. K. **Serum Transaminase Activity in Acute Infective Hepatitis—a Comparison of the Pyruvic and Oxalacetic Transaminases.** *J. Ass. Physicians India.* 1960, Nov., v. 8, No. 6, 520–26. [22 refs.]

The authors estimated the levels of serum glutamic oxalacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) in 50 healthy patients and compared the levels with those found in patients with acute infective hepatitis. The levels in healthy patients ranged from 5 to 40 units per ml. SGOT and from 4 to 30 units for SGPT. In acute infective hepatitis, the levels were from 380 to 670 SGOT and 410–700 units per ml. SGPT in the first week, falling to normal in 5 to 8 weeks: similar levels were found in 2 patients thought to be suffering from anicteric hepatitis. The levels tended to be highest of all in clinically fulminant cases so that estimations of the 2 enzymes may be of value in prognosis. *A. B. Christie*

TARANTAEV, T. M., TOKAR, C. K., KUVSHINNIKOV, S. M., ZUBOVA, E. K., MINEEVA, R. G. & ONISCHENKO, G. P. **Seroprophylaxis of Infective Hepatitis.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1959, v. 30, No. 11, 9–14. [Translated from Russian.]

This field study involving mainly children of pre-school age (2,735 in the test group and 1,015 in the control group) showed that gamma-globulin in doses of 0·14–0·2 ml. per kgm. body weight decreased the incidence of infective hepatitis by 7·1 times, or where the infection was manifest the disease was arrested, conferring a passive immunity which lasted for 7 weeks. Those receiving this dosage within 19 days of being in contact with the disease did not develop the infection. Smaller doses of gamma globulin appeared to reduce the incidence of the disease but did not affect the course of the disease of those already with clinical manifestations of the disease. Anti-measles serum in doses of 30 ml. was not markedly effective but 60 ml. of the same preparation appeared to give results of the same order as the high level doses of gamma globulin (0·14–0·2 ml. per kgm. body weight). The authors conclude that gamma globulin in the correct dosage is valuable in the prophylaxis of infective hepatitis. *H. J. Bensted*

KRUGMAN, S., WARD, R., GILES, Joan P. & JACOBS, A. M. **Infectious Hepatitis. Studies on the Effect of Gamma Globulin and on the Incidence of Inapparent Infection.** *J. Amer. Med.* Ass. 1960, Oct. 15, v. 174, No. 7, 823–30, 5 figs. [12 refs.]

This article gives useful answers to several unsolved problems in infectious hepatitis. Four controlled studies in prophylaxis with gamma globulin were made in an institution for mentally defective children in New York in which the disease had been endemic for the last 7 years. In the first trial a single dose of 0·01 ml. gamma globulin per pound of body weight was followed by a 2½-fold reduction in incidence of hepatitis with jaundice in the patients under test compared with the controls. The same dosage given to adults (attendants) was found to be ineffective. In the second and third trials 0·06 ml. per lb. was followed by a 10-fold and 30-fold reduction of overt jaundice. It was thus clear that the optimum prophylactic dose of gamma globulin is 0·06 ml. per lb. especially for older children and adults.

In a fourth trial a small group of newly admitted patients was studied for evidence of subclinical infection, by the use of the thymol turbidity, cephalin flocculation, and serum transaminase (SGOT) tests of liver function after receiving this dose. The interesting finding in this experiment was that inapparent hepatitis was very frequently present in this community in spite of gamma globulin and would have been undiagnosed but for these tests. The actual ratio of anicteric hepatitis to overt jaundice was 12:1. It would seem that passive-active immunity was being induced among the inmates on a large scale under the conditions of endemic infection present.

Second attacks of hepatitis were observed in 4% to 8% of patients who had had a previous episode of the disease.

[See also this *Bulletin*, 1960, v. 35, 380.]

H. Stanley Banks

HURLBUT, H. S. & THOMAS, J. I. **The Experimental Host Range of the Arthropod-Borne Animal Viruses in Arthropods.** *Virology.* New York. 1960, Nov., v. 12, No. 3, 391–407.

Arthropods were inoculated into the haemocele with 10% infected mouse brain and the whole bodies passaged to similar arthropods by inoculation after 5–10 days at 30°C. Immature arthropods were used except for bedbugs and mosquitoes. The growth of virus in the arthropods was assayed by mouse inoculation, and after passage the viruses were identified by neutralization tests. All the arthropods were from laboratory colonies except the meadow grasshopper (*Conocephalus strictus*). The criterion of success was 5 serial arthropod-arthropod passages. The results are set out in a table:—

ARBOR VIRUSES—ARTHROPOD SPECTRA

Arthropod	Virus*												
	Group A				Group B						Ungrouped		
	EEE	WEE	Sindbis	Semliki	St. Louis E.	W. Nile	Japanese E.	Uganda S.	Niaya	Dengue 1	Phlebotomus F. (S)	Colorado Tick F.	Quaranfil
German roach (*Blattella germanica*)	−	−	−	−	−	−	−	−	−	−	−	−	−
Meadow grasshopper (*Conocephalus strictus*)	+	+	+	+	+	+	−	−	−	−	−	−	−
Bedbug (*Cimex lectularius*)	+	+	+	−	−	−	−	−	−	−	−	−	−
Milkweed bug (*Oncopeltus fasciatus*)	+	+	+	+	−	−	+	−	−	−	−	−	−
Black carpet beetle (*Attagenus piceus*)	+	+	+	−	+	+	+	+	+	−	−	−	−
Indian meal moth (*Plodia interpunctella*)	+	+	+	+	+	+	+	−	+	−	−	−	+
Mosquito (*Culex tarsalis*)	+	+	+	+	+	+	+	+	+	+	+	−	−
House fly (*Musca domestica*)	−	+	+	+	+	+	+	−	−	−	−	−	−
Soft tick (*Ornithodoros savignyi*)	+	+	+	+	+	+	+	+	−	−	−	+	+

* +, Virus propagation demonstrated; −, virus propagation failed.

Bunyamwera virus grew in the bedbug, carpet beetle and mosquito. Viruses of both groups could be recovered from the carpet beetle after periods of up to 303 days at titres from 1·9–6·1 log.

The arthropods were unaffected by these infections and the gross infection characteristics of the viruses were unchanged by passage in them. Serial propagation failed in an isopod (*Armadillidium nastaum*), a slug (*Limax maximus*) and an earthworm, but group A viruses (and not group B) could be recovered from the isopod after 7 days at titres of 3·4–5·0 log. Viruses in both groups were shown to pass through moulting and metamorphosis in several arthropods (bug, beetle, moth, housefly). Western encephalitis virus was found to be concentrated in the thoracic ganglion (titres<3·8–6·2 log) in the grasshopper and a similar predilection for the nervous system was shown in arthropods with some other viruses. Phlebotomus fever virus was passaged 34 times through *Culex univittatus* with a gradual increase in titre; mosquitoes could not be infected by feeding but parenterally infected mosquitoes transmitted by bite. West Nile virus had 17 serial passages in *Argus persicus*. Different mouse-passage levels of several viruses (3–460) did not affect their ability to infect arthropods by inoculation.

The evolution of arthropod-borne viruses in the light of these very interesting findings is discussed. This paper contains a wealth of detail which cannot be abstracted.

C. E. Gordon Smith

HESS, A. D., SMITH, J. V. & LAMOTTE, L. C., Jr. Análisis de las tasas de transmisión de la encefalitis en los estados occidentales de Estados Unidos. [**Encephalitis Transmission Patterns in the Western States**] *Bol. Oficina Sanitaria Panamericana.* 1960, Nov., v. 49, No. 5, 462–6. [15 refs.]

The English summary appended to the paper is as follows:—

"From 1955 through 1959 transmission rates for St. Louis (SLE) and western (WE) encephalitis in the western United States were studied through the use of avian sentinel flocks. These rates appear to exhibit certain regional patterns, with WE usually predominating in the northern zone and both viruses showing high levels of activity in the southern zone. Outbreaks of both SLE and WE occur in the central zone, but transmission of SLE appears to be more sporadic and localized than for WE. Transmission rates for both viruses show marked variations from year to year. A major objective of our investigations on the natural history of encephalitis is to determine the ecological factors that are responsible for these annual and regional differences."

KUZNETSOVA, R. I., SUKHOMLINOVA, O. I. & CHURILOVA, A. A. **The Character of Biphasic Meningo-Encephalitis in the Leningrad Oblast.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 2, 262–8, 3 figs. [Translated from Russian.]

In the Leningrad Oblast' coniferous forest predominates except for parts of the north where the forest is deciduous. These are interspersed with secondary forest due to felling and with pastures and grassland.

Around 59 villages *Ixodes ricinus* predominated, around 48 *I. persulcatus* predominated, and around 7 both species were about equally common. *I. ricinus* predominated in mixed forest of alders, ivy and birch with thick undergrowth and in associated pastures. *I. persulcatus* was mainly in coniferous forest and particularly on the forest edge. *I. ricinus* was mainly in western districts including the Karelian isthmus, *I. persulcatus* in eastern districts.

The tick population is generally of low density (10–15

per man-hour). Tick activity begins about the end of April. *I. persulcatus* reaches maximum activity in May and decreases sharply by mid-June. *I. ricinus* is active throughout the summer and into the autumn.

The Priozerskii District in the north-west of the Oblast' is representative of an *I. ricinus* area: 313 cases occurred during 8 years including a few outbreaks (45, 31 and 13 cases) most of them with biphasic fever, meningo-encephalitis and no paralysis. Virus was isolated from patients' blood, ticks and goats' milk. The Kirishkii District—south-central in the Oblast'—was a typical *I. persulcatus* area. 32 sporadic cases occurred in the 8 years—these were typical encephalitis, 6 with paralysis; 1 patient died. In Districts with a mixed tick population 101 cases were recorded, 31 of them encephalitis and 70 biphasic meningo-encephalitis. Of a total of 371 cases in *I. ricinus* areas none had paralysis: of 74 in *I. persulcatus* areas 15 developed paralysis or paresis.

C. E. Gordon Smith

DANES, L. & BENDA, R. **Study of the Possibility of preparing a Vaccine against Tick-Borne Encephalitis, using Tissue Culture Methods. IV. Immunisation of Humans with Test Samples of Inactivated Vaccine.** *Acta Virologica.* Prague. 1960, Nov., v. 4, No. 6, 335–40, 3 figs.

3 batches of vaccine were prepared from infected fluid from chick embryo cultures 48 hours after infection and were inactivated by formalin (1:2000 final) at 4°C. Sterility and inactivation were checked and potency estimated by immunizing mice with 3 intraperitoneal doses of 0·5 ml. at intervals of 3 and 5 days. The mouse sera were tested for neutralizing antibodies and other mice were challenged intraperitoneally. The infectivity titres of the 3 batches before inactivation were 6·5–7·0 log LD50/0·03 ml., the sera of vaccinated mice neutralized 1·5–2·0 log LD50 and the protective indices of challenged mice were 5·7–6·5 log LD50.

4 volunteers were given 3 doses of 2 ml. in one day followed by similar doses 1 and 6 weeks later. 2 showed good neutralizing antibody responses and 1 was immune before vaccination. 27 volunteers received 3 doses in one day followed by similar doses 2 and 4 weeks later. 26 had neutralizing antibody responses [although in 4 this does not appear to have reached 1·5 log and in 3 others this level was only just attained]. Persons given 0·2 ml. doses intracutaneously appeared [on very small numbers] to react as well as those receiving 2 ml. subcutaneously. Complement-fixing antibody could not be demonstrated in any of the vaccinated persons. No evidence was obtained of sensitization effects due to the vaccine or to its components which were tested in volunteers.

[See also this *Bulletin*, 1960, v. 35, 717.]

C. E. Gordon Smith

ŠIMKOVÁ, A., DANIELOVÁ, V. & BÁRDOS, V. **Experimental Transmission of the Tahyna Virus by *Aëdes vexans* Mosquitoes.** *Acta Virologica.* Prague. 1960, Nov., v. 4, No. 6, 341–7, 1 fig. [10 refs.]

Tahyna virus was isolated from *Aedes vexans* and *A. caspius* in Czechoslovakia [this *Bulletin*, 1960, v. 35, 207]. Two strains isolated from mosquitoes were used; strain 92 after 12–14 mouse passages and strain 236 after 6 extraneural passages in hamsters. The *A. vexans* were bred from field-caught larvae or were caught as adults. In the laboratory they were maintained at 80–90% humidity and 26–30°C.

Mosquitoes were fed on a pledget of wool soaked with 7·5 log LD50 of strain 92: virus was detected daily for 21 days by inoculating ground mosquitoes into mice. The virus titre in mosquitoes was 1·0–2·2 log LD50. Mosquitoes were next infected by feeding on a suckling mouse circulating about 5 log LD50 of strain 236 per mosquito meal. The virus titre in the mosquitoes appeared to fall until the fourth day of incubation then rise to a level of about 4·0 log LD50 which was maintained for at least 30 days. Negative results were obtained with individual mosquitoes on the 3rd, 4th, 7th and 30th days showing that 100% infection was not achieved. Transmission experiments were made by allowing the mosquitoes to feed on 2-day-old mice. 9 of 12 transmission experiments were successful after extrinsic incubation periods of 4–16 days. In one successful experiment only 1 mosquito was used.

C. E. Gordon Smith

SHAH, K. V. & MURTHY, D. P. N. **Investigation of the Possibility of Transmission of Kyasanur Forest Disease Virus from Mother to Child by Milk or across the Placenta.** *Acta Virologica.* Prague. 1960, Nov., v. 4, No. 6, 329–34. [12 refs.]

Because infections with tick-borne encephalitis virus are known to be transmitted in the milk of naturally infected goats, evidence of milk-borne infection in the suckling infants of human patients with Kyasanur Forest disease was looked for. 6 patients and infants were examined. On 3 occasions milk was tested for virus within 7 days of onset and none detected—blood taken at the same time contained virus. 7 milk specimens between the 9th and 14th days and 4 between the 22nd and 44th days of the disease also had no detectable virus. 2 of the 6 children were ill 4 and 12 days after onset of the mother's disease but virus was not isolated from their blood nor was serological evidence found of Kyasanur Forest disease. Sera from 5 of the 6 children were examined but no evidence of infection obtained. One child was born on the 5th day of the mother's illness and she had been shown to have viraemia on the 3rd and 7th day but no evidence of infection was found in the child.

C. E. Gordon Smith.

HADDOW, A. J., DAVIES, C. W. & WALKER, A. J. **O'nyong-Nyong Fever: an Epidemic Virus Disease in East Africa. 1. Introduction.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Nov., v. 54, No. 6, 517–22, 1 map.

During the first half of 1959 a major epidemic of a dengue-like disease broke out in north-west Uganda and spread south-east to cross the Kenya border reaching the Kavirondo Gulf. It is believed also to have spread into the Congo and the Sudan. 750,000 cases without deaths

have probably occurred with fever, headache, severe pains in joints and back, itching rash and adenitis. It has a high attack rate regardless of age or sex. The virus was isolated from patients but was difficult to adapt to mice. It was also isolated from *Anopheles* (*Myzomyia*) *funestus* and *A.* (*M*) *gambiae* in several areas but not from culicine mosquitoes which have been scarce in most of the infected areas. The only disease-free area in one heavily affected region was also the only area in which *A. funestus* and *A. gambiae* were very scarce. The virus has been isolated from mosquitoes kept alive as long as three weeks in the laboratory. The virus has been identified as belonging to group A of arthropod-borne viruses and is related to Chikungunya virus. This paper is an introduction to a detailed series.

C. E. Gordon Smith

TOMCSIK, J. Eine neue serologische Reaktion zur Diagnose der Mononucleosis infectiosa. [**A New Serological Reaction for the Diagnosis of Infectious Mononucleosis**] *Schweiz. med. Woch.* 1960, Dec. 10, v. 90, No. 50, 1444–6. [16 refs.]

The Paul-Bunnell reaction, which is the most frequently used serological test in the diagnosis of glandular fever, is simple to use but its results are not reliable for reasons which are discussed. Newer serological tests in which the many hetero-antibodies to sheep red blood cells present in human serum in health and in disease are first absorbed, give much more reliable results but are complicated and time-consuming.

This paper contains a technical description of a new test in which trypsinized bovine red blood cells instead of sheep cells are tested with the human serum absorbed by means of a guineapig kidney suspension made from dried kidney tissue. Only 5 test tubes are required in the final determination of the agglutinin titre. The specificity of this new and simple serological test is stated to be excellent.

The theoretical advantages of the use of bovine red cells are:—(1) the bovine cells contain definitely more infectious mononucleosis antigen than do sheep red cells, (2) bovine cells contain no Forssman antigen, and (3) haemagglutination of trypsinized bovine erythrocytes can be seen more clearly in the test than that of sheep red cells.

M. E. Delafield

RUGIERO, H. R., CINTORA, F. A., LIBONATTI, E., MAGNONI, C., CASTIGLIONI, E. & LOCISERO, R. Formas nerviosas de la fiebre hemorrágica epidémica. [**Neurological Forms of Epidemic Haemorrhagic Fever**] *Semana Méd.* 1960, Oct. 17, v. 117, No. 33, 1267–72. [22 refs.] English summary.

This is a study of 520 cases of epidemic haemorrhagic fever seen in the neighbourhood of Buenos Aires between 1958 and 1960. This is a disease thought to be due to a virus conveyed by an acarine parasite and is commonest in young adults in rural areas. The usual form is characterized by fever, hypotension and sweats, by petechiae in the soft palate and on the skin and by bleeding from the gums and nose. There are leucopenia and a reduction of platelets to about 40,000 per cmm., a normal or reduced erythrocyte sedimentation rate, the appearance of round cells like the ova of parasites in the urine along with hyaline, granular or blood casts. Nervous complications consisting of headache, insomnia, delirium and trembling are not uncommon. Severe forms may be associated with accentuation of haemorrhagic, renal or nervous manifestations and this article mentions in particular 5 patients who, after apparent recovery, had severe relapses with symptoms of meningoencephalitis. The relapses occurred after 15 to 30 days of normal temperature: all 5 patients recovered rapidly after an illness lasting between 6 to 10 days.

A. B. Christie

BILLO, O. E. & WOLFF, J. A. **Thrombocytopenic Purpura due to Cat-Scratch Disease. Case Reports of Three Brothers who were continuously exposed to Eleven Farm Cats.** *J. Amer. Med. Ass.* 1960, Dec. 3, v. 174, No. 14, 1824–6. [18 refs.]

"A case of thrombocytopenic purpura complicating cat-scratch disease is reported and the pathogenesis discussed. It is thought that the thrombocytopenia is attributable to the basic disease and not to incidental drug therapy."

Bacteriology and Immunity

The order in this section is:—**General; Bacteriostatic and Bactericidal Substances; Bacteria; Rickettsiae; Bacteriophages; Viruses; Immunity.**

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-divisions of this section.*

GENERAL

BLOWERS, R. & CREW, Beryl. **Ventilation of Operating-Theatres.** *J. Hygiene.* 1960, Dec., v. 58, No. 4, 427–48, 8 figs. & 2 pls. [15 refs.]

The ventilation of surgical operating theatres by plenum (positive pressure) systems incorporating air filters has been widely adopted with the object of preventing the entry of contaminated air from other parts of the hospital. But outbreaks of infection, apparently airborne, have sometimes occurred in theatres so equipped. During one such outbreak [this *Bulletin*, 1956, v. 31, 181] it was found that the plenum plant was removing bacteria at only a fraction of the rate at which it was capable. Investigations of other plants revealed great variations in performance, and the variations often seemed to depend on quite small differences of design. Hence the study described in this paper was made with the object of defining the principles that should be observed in designing systems for operating theatres.

Studies were made in 22 theatre suites in different parts of Great Britain. In 10 instances there was exhaust, and in 12 plenum, ventilation. The direction of air flow was studied, and in most of the suites bacteriological studies of the air during actual operating sessions were made. In some instances experimental studies were made after artificial contamination of the air.

It was found that pathogenic bacteria were removed from the air by relatively simple filters having an efficiency of 99·9% for 5μ particles. The air passed through a coarse glass-wool primary filter, and then through 4 Vokes K600 Kompak fabric filters in parallel. This filtration reduced the general bacterial count to such a low level that pathogens were no longer detectable.

To ensure an outward flow of air over the whole area of the doorway when the theatre door is open a flow of at least 33 cu. ft. a minute per sq. ft. of doorway was found necessary. In a conventional system for an operating theatre the plenum fans are supplemented by extraction fans, the rate of extraction being about 75% of the rate of plenum input. With a double door of the usual size the area of the doorway is about 30 sq. ft., so that an outward flow of 1,000 cu. ft. per minute is necessary, but this would be impracticable if the practice of exhausting 75% of the input were observed. Instead, the authors placed exhaust ports in the desired positions and equipped them with pressure-relief flap-valves instead of fans, so that when the doors were closed the valves were opened by the air pressure, but when a door was opened the pressure dropped, the valves closed, and the whole air supply was available to leave through the doorway. This arrangement made it possible to obviate the ingress of contaminated air with an input air flow of 1,200 cu. ft. a minute.

Other rooms in the operating suite should be ventilated in the same way, with flow rates depending on the areas of the doorways. It is also concluded that all openings between the rooms of a suite should be fitted with doors to prevent airborne cross-contamination and high-level loss of ventilating air.

Methods for producing turbulent and displacement ventilation are described, and the relative merits of the two systems are discussed. The evidence that is available seems to be in favour of the downward displacement system.

Attention was paid to thermal comfort. It is concluded that discomfort from overheating was largely due to faulty design and siting of sterilizing equipment.

Thomas Bedford

LIDWELL, O. M. & WILLIAMS, R. E. O. **The Ventilation of Operating-Theatres.** *J. Hygiene.* 1960, Dec., v. 58, No. 4, 449–64, 3 figs.

Measurements to assess the performance of the ventilating system were made in 26 operating theatres. Nitrous oxide was used as a tracer gas to simulate the movement of airborne bacterial contamination. As the principal index of the effectiveness of the ventilation, a quantity referred to as "the exposure to contamination" [this *Bulletin*, 1961, v. 36, 33] was used. This quantity is the integrated product of time and the tracer concentration in the sample of air, and it is expressed in parts per million × minutes, per litre of nitrous oxide liberated. The integration was achieved by collecting the air sample, at a constant rate, into a rubber bag, and then estimating the concentration in the air thus collected. The collection was carried out from the moment of liberation of the tracer gas for a suitable period, usually 10 minutes.

Other observations included the measurement of air speeds at ventilating inlets and outlets, observations of the direction of air currents, and measurements of air temperature and humidity and of radiant heat.

It is concluded that to prevent local clouds of contamination due to the activities of the operating team persisting in the neighbourhood there should be appreciable air movement in the centre of the room. Downward-displacement ventilating systems may be an exception to this, but the indications for the use of these systems are not clear.

The need for limiting the volume of air extracted, if adequate positive pressure is to be maintained in the theatre, is emphasized.

Many complaints were received of uncomfortably hot conditions in the theatres, and almost always the trouble arose from the amount of wild heat fed into the theatre suite from autoclaves and the steam pipes serving them. Such heat dissipation should be avoided.

Thomas Bedford

BLOWERS, R. & BOUND, W. H. **Air Hygiene and Vacuum Cleaners.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1960, Nov., v. 19, 207–11.

The hygienic efficiency of a number of vacuum cleaners was tested by allowing the effluent air to inflate a polythene bag from which air samples could be collected for bacteriological analysis. 2 cleaners with cloth dust collection bags gave effluent air counts of 45 and 105 bacteria-carrying particles per cu. ft.; 1 other with a cloth bag gave 3·4. 7 with paper bags, with or without cloth outer bags, gave counts between 0·8 and 3·2, while 1 which in addition to cloth and paper bags had a glass-wool filter yielded 0·16. Those cleaners in which the effluent emerged in a horizontal jet raised dust off the floor to give increased air bacterial counts. It is concluded that paper collection bags are desirable, and that the exhaust jet should be baffled or diffused.

[See also this *Bulletin*, 1959, v. 34, 149, 921.]

R. E. O. Williams

DIMMICK, R. L. **Characteristics of Dried *Serratia marcescens* in the Airborne State.** *J. Bacteriology.* 1960, Sept., v. 80, No. 3, 289–96, 6 figs. [16 refs.]

Powders prepared from freeze-dried or gel-dried *Serratia marcescens* [*Chromobacterium prodigiosum*] were dispersed into the air of a chamber and the decay rate of the particles was measured by sampling the air with a fluid impinger or a slit sampler. The mass median diameters of the aerosols varied between 6 and 15μ. A period of rapid decrease in the count of viable airborne particles was followed by a period of slower decrease. Loss of viable organisms was rapid at relative humidities above 50% and also in the region of 15%; the longest survival seemed to be at about 0 and at about 30% RH. There was some suggestion that bacteria in dried particles dispersed into the air survive best at low humidities whereas those in wet particles survive best at high humidity. [The extent to which the particles were lost by settling is not fully discussed although some samples were taken with the Andersen particle-size sampler.]

R. E. O. Williams

STEINHAUS, E. A. **Symposium: Selected Topics in Microbial Ecology. II. The Importance of Environmental Factors in the Insect-Microbe Ecosystem.** *Bact. Reviews.* 1960, Dec., v. 24, No. 4, 365–73, 2 figs. [22 refs.]

BERRY, L. J. & SMYTHE, Dorothy S. **Effects of Bacterial Endotoxins on Metabolism. III. Nitrogen Excretion after ACTH as an Assay for Endotoxin.** *J. Exper. Med.* 1961, Jan. 1, v. 113, No. 1, 83–94. [22 refs.]

MADOFF, M. A., EYLAR, E. H. & WEINSTEIN, L. **Serologic Studies of the Neurominidases of *Vibrio cholerae*, *Diplococcus pneumoniae* and Influenza Virus.** *J. Immunology.* 1960, Dec., v. 85, No. 6, 603–13, 4 figs. [19 refs.]

TULASNE, R., MINCK, R., KIRN, A. & KREMBEL, J. Délimitation de la notion de formes L des bactéries: protoplastes, sphéroplastes et formes L. [**Delimitation of the Notion of Bacterial L Forms: Protoplasts, Spheroplasts and L Forms**] *Ann. Inst. Pasteur.* 1960, Dec., v. 99, No. 6, 859–74, 35 figs. on 2 pls. [22 refs.]

The English summary appended to the paper is as follows:—

"The introduction in bacteriology of new words, such as protoplasts and spheroplasts, applying to spherical bodies resulting from bacteria submitted to various influences, might be a source of confusion in the already complex problem of bacterial forms.

"The significance of these different words must therefore be delimited. In agreement with the present-day knowledge, the authors propose the following definitions:

"*Protoplasts:* Spherical bodies issued from bacteria, completely deprived of cell-walls, which do not divide on solid media and are unable to revert to the original bacteria.

"*L forms of bacteria* (a general definition): Spherical bodies resulting from bacteria the cell-wall of which has been modified or completely destroyed by various agents; they may multiply and yield colonies on solid media.

"*L forms of type B* (spheroplasts): Spherical bodies issued from bacteria, with temporarily incomplete cell-walls, multiplying on solid media, able to revert to the original bacteria when the inducing agent has disappeared.

"*L forms of type A:* Spherical bodies issued from bacteria, completely deprived of cell-walls, multiplying on solid media, having lost the factors necessary to reconstitute the original bacteria."

SMITH, P. F. & ROTHBLAT, G. H. **Incorporation of Cholesterol by Pleuropneumonia-Like Organisms.** *J. Bacteriology.* 1960, Dec., v. 80, No. 6, 842–50, 3 figs. [12 refs.]

SMITH, P. F. & BOUGHTON, Janet E. **Role of Protein and Phospholipid in the Growth of Pleuropneumonia-Like Organisms.** *J. Bacteriology.* 1960, Dec., v. 80, No. 6, 851–60, 6 figs. [21 refs.]

INTERNATIONAL ASSOCIATION OF MICROBIOLOGICAL SOCIETIES. SECT. BIOL. STANDARDIZATION. **Fifth International Meeting of Biological Standardization held at The Hebrew University, Jerusalem, September 13–20, 1959.** pp. xiv + 496 + xvi, illustrated. [1960.] Jerusalem: The Weizmann Science Press, 33, King George Avenue, P.O.B. 801, Israel.

This volume contains the scientific contributions of a large number of some 150 participants who attended the 5th International Meeting of Biological Standardization held in Israel in September 1959. It is extremely well produced and arranged and, as an official record of the scientific business of the meeting, is a valuable document. It is more difficult to assess its value as a collection of scientific papers because most of the material presented is not in itself original, but is based on investigations already reported. Nevertheless, the majority of the papers appear to have been specially prepared for submission to the meeting: most of them are fully documented papers set out on standard lines in a form suitable for publication in one of the scientific journals. In a number of instances, after the list of references at the end of the paper, there are one or two paragraphs indicating that there was some sort of discussion afterwards, but there is no suggestion from the proceedings that, where there were several closely related papers, discussions were at all a prominent feature of the conference. With the exception of one paper in German, all the communications are printed either in French or English, but the majority are in English and have been very well prepared. It is not known whether the full text of each paper was delivered as printed, but some are quite long and the total runs to something in the region of a quarter of a million words so that if papers were delivered in full there would have been little time for any extensive discussions.

There were 13 papers dealing specifically with poliomyelitis vaccine and 7 other papers on combined immunization—mainly the quadruple poliomyelitis-diphtheria-tetanus-pertussis vaccine. Only 2 of the polio-vaccine papers considered the live vaccine; V. J. CABASSO and N. R. COX set out the proposed testing requirements (p. 243) and J. L. MELNICK and M. BENYESH-MELNICK submitted an abstract of a paper, published elsewhere, on the increased neurovirulence of the virus after multiplication in vaccinated children (p. 263). The remaining 11 papers were all concerned with the assay of the inactivated vaccine or antibody response to it—G. PENSO (p. 127); R. MURRAY (p. 135); P. LÉPINE, F. ROGER, V. SAUTTER and A. ROGER (p. 157); A. PRINZIE, P. DE SOMER, M. LAMY and E. DE MAEYER (p. 179); E. G. GERWE (p. 197); E. BERGER (p. 213); M. BENYESH-MELNICK and J. L. MELNICK (p. 214); D. R. E. MACLEOD, C. W. J. ARMSTRONG, G. W. O. MOSS, F. C. POTTER and R. J. WILSON (p. 215); T. GOTLEIB and S. LEVENTON (p. 217); A. FOGEL, A. MERCADO, N. GOLDBLUM, P. SKALSKA and L. RANNON (p. 225) and I. SPIGLAND, N. GOLDBLUM, P. SKALSKA and D. MUCHNIKA (p. 233).

The clinical trials of a quadruple vaccine in infants by P. J. WILSON, G. W. O. MOSS, F. C. POTTER and D. R. E. MACLEOD of the Connaught Laboratories, Toronto, is reported in these proceedings (p. 293) in the form of a brief abstract; the full report was published in the *Canadian Medical Association Journal* [see this *Bulletin*, 1960, v. 35, 466], but several tables from Wilson's trials are reproduced in C. MERIEUX's paper on the same subject (p. 267).

Other virus antigen studies include influenza, smallpox and trachoma, among the human virus infections. Immunization against foot-and-mouth disease by standardized vaccine preparations is dealt with in two papers by F. LUCAM and M. FEDIDA (p. 77) and by C. MACKOWIAK, R. LANG, J. FONTAINE, R. CAMAND and H. G. PETERMANN (p. 91). An interesting paper was given by R. A. GOLDWASSER and A. KIMRON (p. 69) on the application of the fluorescent antibody technique for the early detection of rabies virus antigen in the brains of mice following the inoculation of suspect rabies material. Visible staining of the rabies antigen was recorded at least two days before Negri bodies could be demonstrated and several days before signs of infection appeared.

Several papers dealt with qualitative-quantitative aspects of the agar gel precipitation technique (J. G. FEINBERG, p. 355; W. BRAUN, O. J. PLESCIA and N. C. PALCZUK, p. 367; A. L. OLITZKI, J. MARKENSON and M. MARGALITH, p. 375, and E. EYLAN, C. IMRE and J. KEYDAR, p. 383) and there were two proposals put to the meeting by P. BOUQUET and J. G. FEINBERG respectively (p. 389) for the utilisation of the quantitative agar gel plate technique for biological standardization.

There were two papers by British delegates, one by M. STERNE (p. 419) on the standardization of *Clostridium Welchii* and *Cl. botulinum* sera and vaccines and the other by J. UNGAR (p. 425), on the control of the efficiency of freeze-dried BCG vaccine.

It has only been possible to mention some of the subjects dealt with in these proceedings in order to give some idea of the scope covered, but any critical examination of individual papers has not been feasible. The production of this elegant volume reflects great credit on the organization responsible, but it is obvious that the appeal of a publication of this nature must be limited.

The conference itself was widely attended: over 70 of the participants came from countries outside Israel. There were representatives from almost every European country and in addition there were delegates from U.S.A., U.S.S.R., Great Britain, Canada, South Africa, India, Iran and Brazil together with a large attendance from the various research institutes in Israel. *H. J. Bensted*

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

The order in this section is:—**General; Antibiotics; other Therapeutic Substances; Disinfection.**

INNES, A. G. **A Combined Test for Penicillinase Production and Penicillin Sensitivity of Staphylococci.** *J. Applied Bact.* 1960, Apr., v. 23, No. 1, 106–7, 1 fig. on pl.

The author describes a modification of the method of VOUREKA and HUGHES [this *Bulletin*, 1949, v. 24, 525] for the demonstration of penicillin sensitivity and penicillinase production by staphylococci.

Nutrient agar containing 2% of an overnight broth culture of a penicillin-sensitive staphylococcus is poured into a plate from which a ditch is cut and filled with nutrient agar containing 10 I.U. penicillin/ml. Broth cultures of staphylococci under test are streaked across the ditch. After incubation the indicator staphylococcus is seen to be inhibited on either side of the ditch, the edge of the zone of growth being parallel to the ditch.

A penicillinase-producing test strain grows up to, or over the ditch area and there is an arrow-shaped growth of the indicator staphylococcus along the test organism towards the ditch. *M. Patricia Jevons*

YUNIS, A. A. & HARRINGTON, W. J. **Patterns of Inhibition by Chloramphenicol of Nucleic Acid Synthesis in Human Bone Marrow and Leukemic Cells.** *J. Lab. & Clin. Med.* 1960, Dec., v. 56, No. 6, 831–8, 1 fig. [22 refs.]

TISDALE, W. A., FENSTER, L. F. & KLATSKIN, G. **Acute Staphylococcal Enterocolitis complicating Oral Neomycin Therapy in Cirrhosis.** *New England J. of Med.* 1960, Nov. 17, v. 263, No. 20, 1014–16.

"In 4 patients with cirrhosis receiving neomycin by mouth for impending hepatic coma, acute enterocolitis, associated with the appearance of neomycin-resistant *Staphylococcus aureus* in the stools, developed. With omission of the antibiotic and supportive care, recovery was complete in all cases. Enteric infection with *Staph. aureus* during oral neomycin therapy may result from emergence of highly resistant organisms or may be facilitated by neomycin-induced alterations of the bowel itself."

GHIONE, M., BUOGO, A. & SANFILIPPO, A. Attività antibatterica e terapeutica dell'amminosidina nell'infezione sperimentale. [**Antibacterial Action and Therapeutic Value of Aminosidina in Experimental Infections**] *Giorn. di Microbiol.* Naples. 1960, Jan.–Mar., v. 8, No. 1, 9–24, 4 graphs. English summary.

A new antibiotic has been isolated from a species of *Streptomyces* in the Farmitalia Laboratories for Microbiological and Therapeutic Research. It is a white powder, water-soluble and stable in aqueous solution at temperatures just above the freezing point for 7 days, and stable for longer periods at room temperature as a dry powder. It is suitable for parenteral but not for oral administration and it is concentrated by the kidney so that high urinary levels are obtained.

An extensive table of the sensitivity of different bacteria is given, the inhibitory action ranging from 0·02 μgm./ml. for some of the corynebacteria to 400 μgm./ml. for *Proteus mirabilis*. The latter is exceptional. The range of sensitivity for *Escherichia coli* is 2·6 to 17·25 μgm./ml., and is somewhat similar for the anaerobes, but is very marked for the corynebacteriaceae —0·02 to 4·3 μgm./ml. The antibiotic is quite active against the staphylococcus, with a range of less than 0·1 to 13·8 μgm./ml., activity varying considerably with the type of medium used. An action antagonistic to aminosidine is particularly observed in brain/heart infusion broth, and is also exerted by some glucosides and many cations. The streptococcal strains examined proved to be among those most resistant. [The data referred to in the table appear to refer to isolated strains rather than collections of strains and may therefore in some instances be misleading.]

The experiments in producing mutants from cultures grown in the presence of aminosidine have yielded both resistant mutants and some which have become dependent on the presence of the antibiotic. A number of strains of staphylococcus resistant to various antibiotics have been tested and the only strains with considerable resistance are those which had already developed resistance to neomycin. A lesser degree of resistance is shown by strains habituated to antibiotics of similar structure, such as streptomycin and kanamycin.

Among collections of strains of pathogenic bacteria isolated in cases of disease in man, none have been found resistant to aminosidine although strains resistant to most other antibiotics are common.

Experimental observations on the therapeutic activity have been carried out on mice suffering from staphylococcal meningitis and on others infected with tuberculosis. The prolongation of life and lowering of mortality are as good as, or better than, those obtained with other antibiotics.

No action on yeast or fungi has been observed.

J. W. McLeod

LAMENSANS A.; FARI, A. [i] Étude de l'action antibactérienne du sulfamide [**Studies on the Antibacterial Action of Sulphanilamide**] [LAMENSANS & FARI]. *Ann. Inst. Pasteur.* 1961, Jan., v. 100, No. 1, 71–80, 7 figs. [ii] Action du sulfamide sur la synthèse des protéines bactériennes [**Action of Sulphanilamide on the Synthesis of Bacterial Proteins**] [FARI & LAMENSANS]. *Ibid.*, 81–92, 8 figs. [28 refs.]

MATSUSHITA, H., FOX, M. S. & GOEBEL, W. F. **Colicine K. IV. The Effect of Metabolites upon Colicine Synthesis.** *J. Exper. Med.* 1960, Dec. 1, v. 112, No. 6, 1055–68, 6 figs. [12 refs.]

"The synthesis of colicine K by the colicinogenic bacillus *E. coli* K_{235} has been studied in the chemostat.

"It has been found that colicine production is influenced by the pH of the medium, by the nature of the primary carbon source, and by the generation time of the microorganisms."

ŠMARDA, J. **Incidence and Manifestations of Colicinogeny in Strains of *Escherichia coli*.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 2, 151–65, 5 figs. [15 refs.]

VASSILIADIS, P., PAPAVASSILIOU, J., GLAUDOT, A. & SARTIAUX, P. Production de colicines chez les *Salmonella.* (Étude sur 410 souches.) **[Colicine Production by Salmonella. Study of 410 Strains]** *Ann. Inst. Pasteur.* 1960, Dec., v. 99, No. 6, 926–9.

The English summary appended to the paper is as follows:—

"The authors found 11 colicinogenic strains among 410 studied (2,6±0,7 p. 100), including 90 *S. typhi* strains.

"These 11 strains belong to groups B, C_1, E_1, G_2, H and to seven different serotypes: *S. anatum, S. braenderup, S. derby, S. mampeza, S. saint-paul, S. wagenia, S. worthington.* All of them excreted colicin I. There does not seem to exist any strict relationship between antigenic structure and colicinogeny."

DEVRIES, J. A. & SALISNJAK, M. M. **Disinfection of Nurseries contaminated with Staphylococci.** *Canadian Med. Ass. J.* 1960, Nov. 19, v. 83, No. 21, 1082–4, 2 figs.

The routine devised for cleaning contaminated nurseries in a Montreal hospital comprised, first, the spraying into the air of an aerosol of o-benzyl-p-chlorophenol (Aseptone) in propylene glycol and alcohol. When this had settled, the floor, walls and contents of the room were washed with an Aseptone soap mixture. Cultures of areas of wall, etc., showed that this method was effective in ridding the room of staphylococci and some laboratory tests suggest that the addition of the disinfectant to the soap solution had real value. [No tests are reported in which rooms were cleaned without the disinfectant.]

R. E. O. Williams

MEDICAL RESEARCH COUNCIL. **Sterilisation by Steam under Increased Pressure. A Second Communication to the Medical Research Council by the Working Party on Pressure-Steam Sterilisers** [HOWIE, J. W., Chairman]. *Lancet.* 1960, Dec. 3, 1243–4.

The need for high-vacuum dressing sterilizers with an initial vacuum down to an absolute pressure of 20 mm. Hg or less has been confirmed by several members of the working party and this recommendation has now been incorporated in two recent specifications by the British Standards Institution. Many such sterilizers have now been installed in the U.K. and have been found to be mechanically reliable and bacteriologically efficient, but certain minor improvements may still be expected. Attention is drawn to the potentially greater output of the high-vacuum sterilizer as compared with other types of the same cubic capacity.

The report also deals with the need to filter the air used to break the vacuum at the end of the sterilizing cycle. Glass fibre felted into sheet form of paper thickness has been found to be suitable material for the filter, but requires adequate support; it is suggested that the filter material should be held firmly between metal grills which not only give support but prevent distortion and ensure uniform efficiency at all air flows. Air filters built on these lines will have a working life of a year or more, whereas cotton-wool filters, which are not recommended, require frequent changing.

The new high-speed instrument sterilizers are proving to be satisfactory in practice and a British Standard has been published. It is also noted that surgical rubber gloves may be sterilized in a high-vacuum apparatus at 130–134°C. along with dressings without suffering undue damage.

[For the first communication, see this *Bulletin*, 1959, v. 34, 807.] *H. J. Bensted*

KNOX, R., PENIKETT, E. J. K. & DUNCAN, Mary E. **The Avoidance of Excessive Superheating during Steam Sterilization of Dressings.** *J. Applied Bact.* 1960, Apr., v. 23, No. 1, 21–7, 2 figs.

One objection that has been raised to the use of high pre-vacuum in steam sterilizers is that this might lead to excessive drying of dressings with consequent superheating during the period of exposure to steam. This danger has long been recognized when downward displacement sterilizers are used: not only may dressings be damaged or even burst into flame, but sterility may not be achieved because of the poor sterilizing qualities of superheated steam. This paper describes experiments made to determine the degree of superheating attained in a high vacuum sterilizer, by using dressings, techniques and apparatus previously reported by Knox and Penikett [this *Bulletin*, 1958, v. 33, 605]. Thermocouples gave direct readings of the temperature of the dressings under various conditions of sterilization.

The results showed that the degree of superheat was directly related to the initial moisture content of the dressings, and was virtually the same whether downward displacement or high vacuum techniques were used. It was also the same for dressings in packs and in drums. With an initial hydration of 1% or less superheat can be as high as 8°C., which the authors regard as significant. For hydrations of 3–5%, which is the value normally found in the United Kingdom, the superheat is only about 4°C. and this is not considered significant. In dry climates or in centrally heated hospitals they recommend that fabrics should be stored in such a way as to ensure that their hydration before sterilization is not too low. Thus, this paper shows that the use of a high initial vacuum does not increase the risk of superheating, either with drums or packs. *J. C. Kelsey*

STRATFORD, B. C., CHRISTIE, R. & DIXSON, Shirley. **The Disinfection of Hospital Blankets.** *Med. J. Australia.* 1960, Oct. 15, v. 2, No. 16, 621–4. [22 refs.]

"1. A review of the literature on disinfection of blankets is presented.

"2. Experiments using 'Hibitane' in both 1:40,000 and 1:100 concentrations in the final laundry rinse are described. No lasting sterility resulted in either case.

"3. Experiments using formalin vapour to treat 92 used hospital blankets in the presence of high humidity and controlled temperature are described. The average reduction of organisms (less *Bacillus* species) is 96% by this method. The time of exposure to the vapour was 15 minutes.

"4. The conclusion is reached that it is practicable to treat all hospital blankets in use at least once a week by this method. However, obviously soiled or dirty blankets should be referred for laundry treatment."

OLIVER, R. & TOMLINSON, A. H. **The Sterilization of Surgical Rubber Gloves and Plastic Tubing by means of Ionizing Radiation.** *J. Hygiene.* 1960, Dec., v. 58, No. 4, 465–72. [12 refs.]

"Threads were infected with the spores of four species of bacteria and put inside rubber gloves which were sealed into plastic bags and irradiated with electrons or gamma rays. A dose of 1·5 Mrad. killed approximately 99·99% of the spores of each species and a dose of 2·5 Mrad. appeared to give an adequate margin of safety for sterilization. Spores were similarly killed inside plastic tubing and within the lumen of hypodermic needles.

"The tensile strength of the gloves decreased with increasing doses of radiation so that the rough, solution-dipped gloves tested were significantly weaker after 8·0 Mrad., but the smooth gloves tested still complied with the British Standard after 30 Mrad. When vacuum-packed before irradiation, rough gloves were still satisfactory after 16 Mrad., and smooth gloves were apparently unaffected by 30 Mrad.; they could, therefore, be sterilized six and twelve times, respectively.

"Radiation gives dependable sterilization of rubber gloves, and the use of a sealed plastic package obviates subsequent contamination. The possibility of using disposable radiation-sterilized gloves is discussed, the use of a plastic radiation indicator suggested and the practical applications of radiation sterilization in the hospital considered."

BACTERIA

The order in this section is:—**Cocci; Donovania; Mycobacterium; Corynebacterium; Haemophilus; Pseudomonas; Pfeifferella; Enteric Organisms; Brucella; Pasteurella; Bacillus; Anaerobes; Spirochaetes; Erysipelothrix; Listeria; Others.**

INNES, A. G. **Tellurite-Egg Agar, a Selective and Differential Medium for the Isolation of Coagulase Positive Staphylococci.** *J. Applied Bact.* 1960, Apr., v. 23, No. 1, 108–13. [12 refs.]

A medium for the isolation of coagulase positive staphylococci from heavily contaminated material is described. This is a modification of LUDLAM'S medium [this *Bulletin*, 1949, v. 24, 364] and makes use of the fact that about 80% coagulase positive staphylococci produce a zone of opacity round the colony when egg yolk is incorporated into a medium [*ibid.*, 1952, v. 27, 792].

The medium contains mannitol, K_2HPO_4, NaCl, lithium chloride, peptone and Lab Lemco. These ingredients are dissolved in water, the *p*H is adjusted to *p*H 9·2, agar is added and the medium is autoclaved. Before use, 10% of a concentrated egg yolk emulsion and 1% of a sterile 1:400 potassium tellurite are added.

Counts of broth cultures of 12 coagulase positive staphylococci on this medium were in good agreement with counts on control blood agar plates and recovery was better than on Ludlam's original medium and the tellurite glycine agar of ZEBOWITZ *et al.* [*ibid.*, 1956, v. 31, 671].

Most coagulase positive staphylococci gave typical dark grey colonies surrounded by clear or opaque zones in 24 hours, some took 48 hours. The clear zones were produced by the action of the end products of mannitol fermentation on precipitated phosphates. Coagulase negative organisms were either inhibited or grew as small, pale, easily distinguishable colonies.

All enterotoxic strains examined were found to be egg-yolk-positive and the authors suggest that the medium may prove useful in the diagnosis of staphylococcal food poisoning. *M. Patricia Jevons*

MENOLASINO, N. J., with the technical assistance of Barbara GRIEVES & Pearl PAYNE. **Isolation and Identification of Coagulase-Positive Staphylococci on Levine's Eosin-Methylene Blue Agar.** *J. Lab. & Clin. Med.* 1960, Dec., v. 56, No. 6, 908–10.

"Data demonstrating the use of Levine's eosin-methylene blue agar as an aid in the identification of coagulase-positive staphylococci is presented. A total of 308 clinical specimens which contained staphylococci was used for this study. The results show that both the albus and aureus strains of coagulase-positive staphylococci grow as characteristic colorless, pin-point colonies on Levine's eosin-methylene blue agar. Comparative studies with Levine's eosin-methylene blue, tellurite-glycine agar, and the plasma coagulase test indicate that Levine's eosin-methylene blue agar appears to be a more sensitive differential medium for presumable pathogenic staphylococci than the tellurite-glycine agar, and also, that there is good correlation between the plasma coagulase test and the growth of coagulase-positive staphylococci on the Levine's eosin-methylene blue agar."

KRETZSCHMAR, W. & WITT, Maria. Der Kristall-violett-test nach Epstein und seine Brauchbarkeit im Rahmen eines biologischen Typisierungs-systems für Staphylokokken. [**Epstein's Crystal Violet Test and its Usefulness in the Formation of a Typing Scheme for Staphylococci**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1960, Sept., v. 6, No. 9, 593–8. [40 refs.]

The colour of a confluent growth on staphylococci on media containing 1/150,000–1/300,000 crystal violet can be used as an additional factor in characterizing strains of *Staph. aureus.* A "typing" scheme can be constructed by the use of this test with the coagulase, egg yolk and mannitol fermentation tests. [However, of 246 strains tested by the 4 methods 178 fell into 1 type, 30 into a 2nd and 13 into a 3rd.] *R. E. O. Williams*

RICHOU, R., RICHOU, R. (Mme), QUINCHON, C. & PANTALÉON, J. Sur la présence, dans les filtrats le culture du staphylocoque, d'enzymes attaquant les lidipes (graisse neutre, ovolipides, lécithine) et la caséine. [**The Presence in Culture Filtrates of Staphylococci of Enzymes attacking Lipids (Neutral Oils, Egg Lipid, Lecithin) and Casein**] *Rev. d'Immunologie.* 1960, July–Sept., v. 24, No. 4, 496–504. [Refs. in footnotes.]

59 culture filtrates were obtained by growing 17 different strains of staphylococci in papain-digested meat broth in an atmosphere containing 20% CO_2.

Petri dishes containing a peptone-salt-agar medium in which were also incorporated the appropriate substrates were used as an assay system. Dilutions of the culture filtrates (in 0·05 ml. amounts) were placed in cups cut in the medium and the dishes then incubated 24 hours at 45°C. The end point was recorded as the highest dilution showing the appropriate visual effect. Filtrates of 16 of the strains gave a positive reaction with egg-yolk [this *Bulletin,* 1952, v. 27, 792] which was apparently associated with the presence of a lipase. Lecithinase activity was completely absent in these filtrates. In contrast, when 15 filtrates prepared from the strain Wood were examined [the method of preparation is not stated] 7 produced a clearing on an egg yolk plate associated with the presence of a lipase, while the remainder produced a zone of precipitation on the egg yolk medium and possessed lecithinase activity. *H. Gooder*

RICHOU, R., QUINCHON, C. & RICHOU, R. (Mme). Sur la présence, dans les sérums sanguins humains et animaux, de principes capables de neutraliser certaines propriétés enzymatiques des toxines staphylococciques. [**The Presence in Human and Animal Sera of Agents capable of Neutralizing Enzymic Activities associated with Staphylococcal Toxins**] *Rev. d'Immunologie.* 1960, July–Sept., v. 24, No. 4, 505–11.

Numerous animal sera were tested for the ability to inhibit the various enzymic activities [described above] of staphylococcal culture filtrates. The sera tested comprised human (33), bovine (18), sheep (33), horse (24), rabbit (15) and dog (3). In general the bovine, sheep, horse, rabbit and dog sera had little ability to inhibit the egg yolk, lipase or lecithinase activity. Among human sera however 11 sera inhibited the egg yolk reaction, 3 the lipase activity and 3 (out of 15 tested) the lecithinase action. Ability to inhibit the digestion of casein by the filtrate was a property of many of the sera and it was suggested this may be a non-specific effect.

H. Gooder

DULANEY, Anna D., CALDWELL, M. G., HANCOCK, J. C., Jr. & BERTON, W. M. ***Staphylococcus aureus*: Bacteriophage on Paper Disks.** *J. Lab. & Clin. Med.* 1960, Nov., v. 56, No. 5, 777–9.

A preparation of phage 80 [of unstated concentration] was applied to discs cut from thin filter paper and dried in a vacuum desiccator. When the discs were placed on agar plates spread with susceptible staphylococcus and incubated for 4 hours at 37°C., a zone of clearing appeared under and 1–1·5 mm. around the disc. On the basis of this experiment it is proposed that similar discs could be used for routine phage typing of stapylococci. [In the reviewer's opinion the experience is quite inadequate as the basis for such a recommendation, and the method hardly seems likely to be capable of providing accurate results.] *R. E. O. Williams*

ISHIHARA, K., TANAKA, A. & TAJIMA, S. **Phage-Typing of Staphylococci from Pyogenic Lesions and Carriers in and Outside the Hospital.** *Japanese J. Microbiol.* 1959, Oct., v. 3, No. 4, 427–42. [20 refs.]

The paper reports the phage typing results from strains of *Staphylococcus aureus* examined in Gunma University, Japan, in 1957–59. Of 128 strains from lesions developing in hospital, 56 were type 80; 15 had other group I patterns, 5 were in group II and 5 in group III. Of 230 strains from lesions developing outside hospital, 15 were type 80 and 29 had other group I patterns; 68 were group II and 15 group III. 93% of the hospital strains were penicillin-resistant and 70% streptomycin-resistant; for the non-hospital strains the percentages were 72 and 28.

Of 120 members of the hospital staff, 98 were carriers of *Staph. aureus* and of the 139 strains isolated from these persons 16 were type 80. No type 80 was identified among 61 strains from new student nurses before admission to the wards; 5 were found among 36 from the nurses after 2–4 months in the wards.

Different phage types seemed to differ in their ability to produce particular lesions. *R. E. O. Williams*

BLAIR, J. E. & CARR, Miriam. **Distribution of Phage Groups of *Staphylococcus aureus* in the Years 1927 through 1947.** *Science.* 1960, Oct. 28, v. 132, 1247–8.

The authors phage typed 256 strains of coagulase positive staphylococci isolated in their laboratory between

August 1927 and December 1947 and 20 strains isolated by other workers during that time, employing the set of typing phages in present use. These strains had been isolated from pathological material and kept for various reasons.

Strains of type 80/81 have only been recognised since 1955 when phage 80 was described by ROUNTREE and FREEMAN [this *Bulletin*, 1956, v. 30, 334]. Because of the current epidemiological importance of strains of this and related types it was thought to be of interest to find out if strains of this type were present as far back as 1927 and in the early years of penicillin therapy.

Of the 276 strains 32·5% were group I; 21·6% Group II; 8·8% Group III; 4·6% Group IV; 2·6% type 187; 22·1% type 80/81; 7·7% mixed types; and 29·7% were non-typable. This type distribution is similar to that reported by WILSON and ATKINSON in 1945 [this *Bulletin*, 1945, v. 20, 579]. The low incidence of Group III strains in both series is in contrast to the predominance of strains in this group after the introduction of antibiotics when resistant strains were first demonstrated in Group III.

43 strains were lysed variously by phages 52/52A/80/81 either at routine test dilutions [RTD] or RTD × 1,000. 14 of these were 52/52A/80/81; 15 strains 52/52A/80; 7 strains 52A/80; 1 strain 52/80; 1 strain 80/81; 2 strains 80; 3 strains 81. 49 of all strains were isolated between 1944 and 1947. 7 of these belonged to the 52/52A/80/81 group and 6 of these were sensitive to penicillin. One penicillin-resistant strain of type 52/52A/80 was isolated from a lesion after 1 month antibiotic treatment. A sensitive strain of the same type had been isolated before treatment.

The authors do not claim that their figures necessarily give the true distribution of staphylococcal types between 1927 and 1947, but they have been able to demonstrate that strains of the present epidemic type 80/81 and its related types were causing staphylococcal disease at that time. *M. Patricia Jevons*

(i) MALTMAN, J. R., ORR, J. H. & HINTON, N. A. **The Effect of Desiccation on *Staphylococcus pyogenes* with special reference to Implications concerning Virulence.** *Amer. J. Hyg.* 1960, Nov., v. 72, No. 3, 335–42, 1 fig. [14 refs.]

(ii) HINTON, N. A., MALTMAN, J. R. & ORR, J. H. **The Effect of Desiccation on the Ability of *Staphylococcus pyogenes* to produce Disease in Mice.** *Ibid.*, 343–50. [26 refs.]

(i) A broth culture of *Staphylococcus aureus* was dried on to the surface of glass tubing. At intervals pieces of the tubing were placed in various fluids and the staphylococci resuspended in them. With increasing duration of storage the number of viable cells recovered from the glass tube decreased, from $8{\cdot}35 \times 10^8$ per ml. at the start to $0{\cdot}62 \times 10^8$ after 14 days. Over the same period the ability of the resuspended cells to survive when held in water, saline or broth at 7°C. or 37°C. decreased. There was also a regular increase in the lag period after resuspension into broth held at 37°C. and a decrease in the rapidity with which the resuspended cells could clot plasma.

(ii) Staphylococci, resuspended from glass after various periods of drying, were tested for their ability to establish lesions on intramuscular, intravenous, or intracerebral injection into mice. In all cases the resuspended staphylococci were less "virulent" than fresh cocci, allowance being made for the decrease in viable count during the drying.

These results are discussed in relation to the current emphasis on contamination of the environment in studies of hospital cross-infection. The analogous findings of PERRY *et al.* [this *Bulletin*, 1957, v. 32, 1196] on streptococci are recalled. *R. E. O. Williams*

NAUMANN, G. Untersuchungen über die Beziehung zwischen Antibiotikaempfindlichkeit und Hämolysinaktivität bei Staphylokokken. [**The Relation of Sensitivity to Antibiotics and Haemolysin Activity in Staphylococci**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 4, 461–6. [23 refs.]

The English summary appended to the paper is as follows:—

"In 141 strains of Staph. aureus the alpha-hemolysin production was determined and compared with the sensitivity to penicillin, streptomycin, and chloronitrin. Only the inhibiting concentration of penicillin showed a negative correlation of a probability of 99 per cent to the hemolysin activity of the strains tested."

ASHLEY, D. J. B. & BRINDLE, M. J. **Penicillin Resistance in Staphylococci isolated in a Casualty Department.** *J. Clin. Path.* 1960, July, v. 13, No. 4, 336–8, 1 fig. [13 refs.]

Antibiotic sensitivities are recorded on 118 strains of coagulase positive staphylococci obtained from cases of minor infection in patients attending the casualty department of a Liverpool hospital between April and June 1959. Swabs were taken at first attendance or at the time of incision, and it is believed that the infections were not contracted in hospital.

Of all strains 46% were resistant to penicillin, 12% to streptomycin, 7·5% to tetracycline. All strains were sensitive to chloramphenicol and erythromycin. In 26 instances patients had been treated with penicillin and 69% of strains from these patients were resistant to penicillin compared with 39% from patients who had not received the antibiotic.

The authors suggest that tetracyclines should be used for the treatment of staphylococcal infections in general practice and the casualty department when the infecting staphylococcus is unlikely to be a hospital "epidemic" strain. *M. Patricia Jevons*

BOGER, W. P., FRANKEL, J. W. & GAVIN, J. J. **Detection and Titration of *Staphylococcus aureus* Agglutinin in Serum.** *Proc. Soc. Exper. Biol. & Med.* 1960, Aug.–Sept., v. 104, No. 4, 639–42, 2 figs.

The test described comprises the mixing of serum dilutions with a living culture of a staphylococcus, overnight

incubation, and the observation of an agglutination pattern in the tube. [In one place the "viability end point" is referred to but this is presumably a misprint.] Most human sera showed an agglutinin titre of 1/1,600 to 1/6,400; a few animal sera had titres of 1/409,600 or more. The titre increased after a course of immunization with a phage-lysed staphylococcus.

R. E. O. Williams

LAMBERT, H. P. **Gamma Globulin in Experimental Staphylococcal Infections.** *J. Lab. & Clin. Med.* 1960, Nov., v. 56, No. 5, 701–10, 5 figs. [15 refs.]

The injection of 0·2–1·0 ml. gamma globulin, shown to contain about 20 units per ml. staphylococcus antitoxin had no effect on the rate of development or ultimate size of skin lesions produced by the intradermal injection of 10^6–10^8 *Staph. aureus*, given with 2 μgm. adrenaline. Erythromycin given up to 2 hours after the staphylococci reduced the size of the lesion; gamma globulin had no synergic effect with the erythromycin. Intraperitoneal injection of 1,000 units of antitoxin also had no effect on the skin lesion. Antitoxin had a slight delaying effect on the development of disease following intraperitoneal inoculation of mice, but gamma globulin had none, probably because of its low antitoxin titre.

R. E. O. Williams

HALBERT, S. P. & AUERBACH, T. **The Use of Precipitin Analysis in Agar for the Study of Human Streptococcal Infections. IV. Further Observations on the Purification of Group A Extracellular Antigens.** *J. Exper. Med.* 1961, Jan. 1, v. 113, No. 1, 131–58, 11 text figs. & 2 figs. on 2 pls. [23 refs.]

"Studies on the purification of group A streptococcal extracellular antigens detectable with naturally occurring human antibodies from normal individuals have been extended. It has been shown that streptococcal electrophoretic fractions intermediate between the most rapidly migrating components are quite complex. In the calcium phosphate chromatography of adjacent electrophoretic fractions, particular antigenic components desorbed at similar buffer elution steps.

"It is clear from the results obtained that substantially more extracellular antigens than the twelve heretofore recognized are secreted in human beings during infection, as judged by their detection with human antibodies. The precise number is not yet known, but is probably greater than 16.

"Of the nine components which thus far have been separated rather well from the others, four were previously identified as streptolysin 'O,' diphosphopyridine nucleotidase, proteinase precursor, and desoxyribonuclease B. The accumulated data substantiated these previous identifications.

"The identity of a fifth antigen has been made as a possible complex of C carbohydrate and protein. Tentative evidence for the relationship of a sixth component to scarlet fexer toxin has been presented.

"It has been shown that rechromatography of crystalline proteinase precursor and desoxyribonuclease B on calcium phosphate columns resulted in elution principally at the expected stepwise increase in buffer concentration.

"Attempts to isolate antigens present as mixtures in some calcium phosphate chromatographic peaks, by rechromatography on DEAE or CM cellulose columns resulted in only limited further purifications."

CREMER, Natalie & WATSON, D. W. **Rash Induction by Intracellular Products of Group A Streptococci.** *Proc. Soc. Exper. Biol. & Med.* 1960, Aug.–Sept., v. 104, No. 4, 570–73, 3 figs. [13 refs.]

A washed suspension of group A streptococci was disintegrated by sonic oscillation and separated by starch electrophoresis. Its fractions were studied; 8 of them reacted with a specific anti-M serum. The extracts and several of the fractions, after intradermal injection into rabbits, produced the nodular lesion described by SCHWAB and CROMARTIE [this *Bulletin*, 1959, v. 34, 679; 1960, v. 35, 694]. Some rabbits also showed a spreading erythematous lesion. Both the nodular and the erythematous lesion tended to recur. When crude sonic extracts were spun at 105,400 g. the sediment was the more active in producing the nodular lesion, while the supernatant fluid produced the erythematous reaction. *R. E. O. Williams*

OTTOLENGHI, Elena & HOTCHKISS, R. D. **Appearance of Genetic transforming Activity in Pneumococcal Cultures.** *Science.* 1960, Oct. 28, v. 132, 1257–8, 2 figs. [12 refs.]

A deoxyribonucleate-containing material with genetic transforming activity was found in cell free filtrates of pneumococcal cultures. The amount of active transforming material present in such filtrates was related to the growth phase, maximum activity appearing at about the middle of the logarithmic phase. In this culture, separate experiments showed that the transformability of the pneumococcus by exogoneous deoxyribonucleate varied in a similar manner. A mixed culture of two strains (one resistant to amethopterin and sulphonamide, the other to streptomycin and micrococcin) was then studied and it was found that each strain was able during growth to donate both of its markers and to accept both markers from the other strain. Mixed cultures thus gave rise to recombinants. *H. Gooder*

HEIDELBERGER, M. & REBERS, P. A. **Immunochemistry of the Pneumococcal Types II, V, and VI. I. The Relation of Type VI to Type II and other Correlations between Chemical Constitution and Precipitation in Antisera to Type VI.** *J. Bacteriology.* 1960, Aug., v. 80, No. 2, 145–53. [Numerous refs.]

Immunochemical aspects of the relation between pneumococcal types II and VI were investigated by means of quantitative precipitin tests employing as antigens numerous gums of known composition and purified specific polysaccharides of types II(SII), VI and XIV; 6 horse antisera were studied, 3 prepared against type II

pneumococci and 3 against type VI. Large differences were found between the 3 type VI anti-pneumococcal sera in the amount of cross precipitation given with SII and also with the gum preparations. From the known composition of the gums and polysaccharides, the type specificity of pneumococcus type VI was resolved into partial specificities due to multiple residues in the long phosphate-linked polysaccharide chain, of 1,3 linked L-rhamnose, 1,3 linked D-glucose and 1,2 bound D-galactose.

The relationship of the type II and type VI polysaccharides was shown to be due to the presence in each of multiple 1,3 linked L-rhamnose residues. *H. Gooder*

KENNER, B. A., CLARK, H. F. & KABLER, P. W. **Fecal Streptococci. II. Quantification of Streptococci in Feces.** *Amer. J. Pub. Health.* 1960, Oct., v. 50, No. 10, 1553–9.

The median density of streptococci in millions per gm. of moist faeces was 1·3 for cow, 3·0 for human beings, 3·4 for fowl, 38·0 for sheep and 84·0 for the pig. Enterococci densities were 0·16, 2·29, 2·10, 9·42 and 8·40 millions per gm. respectively. The enterococcus group on a percentage basis is low in animal faeces, but it cannot be used as a differential procedure from human pollution since, on a daily basis, more enterococci are discharged per animal than by the average person.

A careful classification of the streptococcal groups permits a qualitative interpretation of the possible sources of pollution. The enterococcus group used as an indicator of pollution yields from 77% of the total streptococci from human pollution to as low as 10% from pig faeces. The faecal streptococci, based on results of this investigation, consisted of the enterococcus group, *Strep. mitis-salivarius* group, *Strep. bovis* group, *Strep. equinus* group, and an atypical group closely resembling the enterococcus group, but with one or more differences in critical biochemical tests. Sufficient data have been accumulated to justify further investigations in the distribution of the faecal streptococci for application to the interpretation of pollution problems. The description as faecal streptococci rather than enterococcus is suggested. *E. Windle Taylor*

REDMOND, W. B. & CATER, J. C. **A Bacteriophage Specific for *Mycobacterium tuberculosis*, Varieties *hominis* and *bovis*.** *Amer. Rev. Respiratory Dis.* 1960, Dec., v. 82, No. 6, 781–6, 2 figs. [17 refs.]

Phages which lyse human tubercle bacilli have been isolated on several occasions [see for instance, TAKEYA *et al.*, this *Bulletin*, 1960, v. 35, 1037] but they all lyse other mycobacteria, including saprophytic strains, and none has been found to be specific for pathogens. This paper reports the isolation of a phage, DS6A, which was tested on 300 strains of mycobacteria including avian, vole, saprophytic and unclassified strains but which only lysed human and bovine varieties of *Myco. tuberculosis*.

Phage DS6A was isolated from soil, from a stockyard, which had been incubated with a broth culture of a saprophytic strain (ATCC 607) and then with *Myco. tuberculosis* H37Rv. Electron micrographs of the phage showed it to have a head diameter of 80 mμ and a tail length of 225 mμ. Bacilli made resistant to streptomycin, PAS, isoniazid or cycloserine did not change in their susceptibility to the phage. Plaques produced on bovine strains were slightly more turbid than those on H37Rv. A plaque type variant, DS6B, did not lyse 3 recently isolated human strains which were lysed by DS6A. DS6B was not serologically different from DS6A. The possibility of adapting phages to different strains for typing purposes is discussed. *Janice Taverne*

HIRSCH, A., CATTANEO, C. & MAGGINI, P. Über den Aufbau der Mycobakterien. IV. Zur Frage der Bedeutung der Lipoide in der Struktur der Mycobakterienzellen. (Versuch einer funktions biologischen Deutung elektronen-optischer Untersuchungen.) **[The Structure of Mycobacteria. IV. The Significance of Lipoids in the Structure of Mycobacteria Cells. (Attempt at a Functional-Biological Explanation of Electron-optic Investigations)]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 3, 357–71, 5 figs. [50 refs.]

AOYAGI, T., NOJIMA, S., KONDO, E. & MIZUNO, D. **The Native Constituents of Acetone Soluble Neutral Fats of *Mycobacterium tuberculosis* BCG.** *Japanese J. Med. Sci. & Biol.* 1960, June, v. 13, No. 3, 101–11, 6 figs. [23 refs.]

KONDO, E. **Chemistry of Phosphatide and Wax D of *Mycobacterium tuberculosis* BCG in One Week Culture.** *Japanese J. Med. Sci. & Biol.* 1960, June, v. 13, No. 3, 113–19, 3 figs. [10 refs.]

TSUMITA, T., AOYAGI, T., MATSUMOTO, R., KONDO, E. & MIZUNO, D. **On the Factionation of Complex Components of *Mycobacterium tuberculosis* and their Biological Properties.** *Japanese J. Med. Sci. & Biol.* 1960, June, v. 13, No. 3, 121–9, 1 fig. [19 refs.]

TSUMITA, T., MATSUMOTO, R. & MIZUNO, D. **Chemical and Biological Properties of the Hemagglutination Antigen, a Lipopolysaccharide, of *Mycobacterium tuberculosis* var. *hominis*.** *Japanese J. Med. Sci. & Biol.* 1960, June, v. 13, No. 3, 131–8, 2 figs. [14 refs.]

MATSUMOTO, R. **Chemical and Biological Properties of a Lipopolysaccharide of BCG responsible for Hemagglutination Reaction.** *Japanese J. Med. Sci. & Biol.* 1960, June, v. 13, No. 3, 139–45, 2 figs.

KUBALA, E. **The Influence of Growth-Stimulating Factors on the Bacteriotropic Potencies of Isoniazid.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 2, 191–5, 5 figs.

In these experiments H37Rv and a variant resistant to 500 μgm. isoniazid per ml. were grown in Long medium

containing 0·01 μgm. isoniazid per ml. and 200 μgm. para-aminobenzoic acid (PAB) per ml., and at intervals up to 4 weeks the amount of growth was determined by collecting, drying and weighing the bacilli. The results showed that although when alone PAB increased the rate of growth, it had no effect on the final quantity of growth. In the presence of isoniazid, however, this concentration of PAB not only enhanced the activity of the drug against the sensitive strain, shown by a lower yield of bacilli, but it also decreased the yield of the resistant variant.

In experiments in the Warburg apparatus, this concentration of PAB decreased the uptake of oxygen by H37Rv, in spite of its increasing the growth rate, whereas isoniazid increased the respiration although it decreased the growth rate.

Administration of PAB together with isoniazid to man and animals has been shown to increase the concentration of isoniazid in the blood, and this has been explained by assuming that there is competitive acetylation between PAB and isoniazid; the author, however, does not consider this is the explanation for PAB increasing the activity of isoniazid *in vitro*, especially as the increase occurs also with the highly isoniazid-resistant variant. He considers the increased activity more likely to be due to the stimulating effect of PAB on the growth rate of the tubercle bacillus. *S. R. M. Bushby*

Noufflard, Henriette & Berteaux, Solange. **An Increased Effect with Increased Dosage of Isoniazid in Experimental Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1960, Oct., v. 82, No. 4, 561–3, 1 fig.

McCune and associates have shown that once a certain level of isoniazid dosage has been obtained the phenomenon of microbial persistence of tubercle bacilli in the spleens of infected mice remained uninfluenced by a 5-fold further increase in isoniazid dosage [this *Bulletin*, 1958, v. 33, 514]. This was based on experiments in which the isoniazid was given about the same time as the mice were infected [*ibid.*, 1957, v. 32, 699, 700]. In the present paper increased dosage was given in two different ways: (1) As in the McCune experiments at the time of infection, and (2) in which the use of the isoniazid was postponed until the 20th day after infection. The isoniazid was given by the intracutaneous route as in sick animals the alimentary route was found to be unreliable.

In the group treated at the time of infection an increased dosage up to 10 mgm. per kgm. daily dosage produced an appreciable improvement, but no further improvement was shown when the dose was increased to 50 mgm. per kgm. per day, though if the observation time was sufficiently prolonged some improvement was obtained. When treatment was postponed it was found that increase of dosage up to 100 mgm. per kgm. per day resulted in a definitely superior effect. The author agrees with McDermott (*Bacterial and Mycotic Infections in Man*, Philadelphia, 1958, J. B. Lippincott Co.), that effective concentration represents an abstraction and the dosage of any drug should be as large as can be administered without entailing serious risk of drug toxicity.

F. H. Young

David, H.; De Alemquer, M. Études sur les bacilles de la tuberculose résistants à l'isoniazide. I. Introduction et comportement *in vitro*. [**Studies on Tubercle Bacilli Resistant to Isoniazid. I. Introduction and Behaviour *in vitro***] [David & De Alemquer]. *Acta Tuberculosea Scandinavica.* 1960, v. 39, No. 3, 172–84, 1 diagram. [Numerous refs.] II. Pouvoir pathogénique pour le cobaye. [**II. Pathogenic Power for Guineapigs**] [David & De Alemquer]. *Ibid.*, 185–93, 3 figs. on 2 pls. [19 refs.] III. Pouvoir pathogénique pour l'homme. [**III. Pathogenic Power for Man**] [De Alemquer & David]. *Ibid.*, 194–202. [31 refs.]

These studies were made on 2 groups of tubercle bacilli, resistant to 5 μgm. isoniazid per ml. The first group consisted of 22 strains which had been grown twice on media containing 5 μgm. or more isoniazid per ml., and were therefore presumed to contain no sensitive bacilli. The second group consisted of 204 strains from 14 patients; these cultures had been grown only once in the presence of 5 μgm. isoniazid per ml. and therefore probably contained some less resistant bacilli.

A comparison of the catalase activity, the presence of the cord-factor and the neutral red reaction of the strains of the first group showed that they varied in their reactions to the first 2 tests but only 1 was positive by the neutral red test. This almost complete uniformity in giving a negative neutral red reaction contrasted strongly with the very variable results with the second group; 63% of these cultures gave a positive reaction, and they also varied in catalase activity and in ability to decolorize dichlorophenolindophenol.

The second paper describes the results of injecting the strains of the first group of bacilli into pairs of guineapigs. The animals were injected into the inguinal region with 1 mgm. of the wet bacilli, and they were killed 7 weeks later. They were then classified according to the extent of tuberculosis; those with no evidence of the disease were placed in class 1, those without disease except at the injection site into class 2, and the remainder into classes 2–5, depending on the extent of the generalized disease. Of the 30 guineapigs inoculated with catalase-positive strains, 26 were placed in classes 4 and 5, whereas of the 14 animals inoculated with catalase-negative strains only 3 fell into these classes. Of the 18 animals inoculated with cord-positive strains, 13 were placed in classes 4 and 5, but so were 16 of the 26 inoculated with the cord-negative strains. Therefore, better correlation was found between catalase activity and virulence than between cording or the neutral red reaction and virulence. Microscopic examination showed, however, that the catalase-status of the bacilli had little effect on the histological appearance of the lesions.

The third paper deals with the course of the disease in the 36 patients from whom these strains were isolated; the patients had been treated with isoniazid, PAS and streptomycin for 12–51 months before the resistant strains were isolated. 5 patients ceased to excrete bacilli after surgical treatment, and 2 others became sputum-negative after 3–4 years' chemotherapy. 20 patients died; 14 of these had excreted catalase-positive strains, and of these, 9 were considered to have died from toxaemia, as

compared with only 1 of those that had excreted catalase-negative strains. Cavities developed in 5 patients after resistance was detected, and in 4 of the patients the strains were catalase-positive; 4 of these patients died and the fifth patient was gravely ill. The remaining 8 patients have very extensive lesions and 4 are excreting catalase-positive strains.

The authors conclude that these findings suggest that the isoniazid-resistant catalase-negative strains are not only attenuated for guineapigs but also for man.

S. R. M. Bushby

TSUKAMURA, M. **Further Mutational Studies on the PAS Resistance of *Mycobacterium tuberculosis* var. *hominis*.** *J. General Microbiol.* 1960, Oct., v. 23, No. 2, 203–8.

In these studies a single colony of H37Rv was grown on Ogawa's egg medium, and the growth suspended in saline. 10-fold dilutions were then prepared and inoculated on to a set of media containing graded concentrations of PAS from 0·1 to 1·0 μgm. per ml. Counts of the colonies growing after 4 weeks' incubation showed that the proportion of bacilli growing in the presence of the PAS did not fall continuously, for a large fall occurred between the concentration of 0·1 and 0·2 μgm. PAS per ml.

The population structure of the bacilli growing in the presence of 0·1, 0·3, 0·5, 0·7 and 1·0 μgm. per ml. was then examined by culturing 2–5 colonies and then determining the proportion of bacilli which would grow in concentrations of PAS ranging from 0·3 to 10 μgm. PAS per ml. The results showed that whereas there was no growth from the colony derived from the 0·1 μgm. PAS per ml. culture and from some of those from the 0·3 μgm. per ml. culture, the remaining colonies from the 0·3 μgm. per ml. cultures and those from the 0·5, 0·7 and 1·0 μgm. per ml. culture grew similarly in concentrations up to 2–3 μgm. per ml., indicating that they were of the same genotype.

At rates of about 10^{-6}, survivors which could grow in 10 and 100 μgm. per ml. were isolated from the colony selected from the cultures containing 1·0 μgm. PAS per ml., and a population study showed that these survivors were identical and could grow in concentrations of PAS from 500 to 1,000 μgm. per ml. Independent tests with other colonies derived from colonies growing in the presence of 10, 100 and 2,000 μgm. PAS per ml. showed that their populations were similar to those derived from the tube containing 0·3 μgm. per ml. In this study no bacillus was found that grew in the presence of 3,000 μgm. PAS per ml.

These results are interpreted as showing that 2 genotypes determine PAS resistance and that both are produced by mutation from the sensitive phenotypes which grow in concentrations up to 0·2 μgm. PAS per ml.; one of the genotypes is responsible for the phenotypes resistant to concentrations up to 3·0 μgm. per ml. and the other to those resistant up to 2,000 μgm. per ml.

S. R. M. Bushby

JENEY, E. & ZSOLNAI, T. Versuche zur Entdeckung neuer Tuberkulostatika. XIII. Die mit Aldehyden und Ketonen gebildeten Derivate von verschiedenen Säurehydraziden. **[Investigations concerning Discovery of New Tuberculostatic Drugs. XIII. Aldehyde and Ketone Derivatives of Acid Hydrazids]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 3, 398–401. XIV. Die *in vitro* ausgeübte tuberkulostatische und auf die experimentelle Meerschweinchen-Tuberkulose ausgeübte antituberculotische Wirkung organischer Schwefel-Verbindungen. **[XIV. Organic Sulphur Compounds, their Antituberculous *in vitro* Action, and their Therapeutic Effect in Experimental Tuberculosis of Guineapigs]** *Ibid.*, 402–10. [11 refs.]

The English summaries appended to the papers are as follows:—

I. "The authors synthesized 52 different acid hydrazides or acid hydrazones. The anti-tuberculous action of these compounds was examined *in vitro*. The hydrazones of undecylic acid, anthranylic acid and cinnamic acid proved to exert a marked activity. It is supposed that this action is a specific one."

II. "The antituberculous *in vitro* action of 100 organic sulfur compounds has been tested. It could be shown that some of them (e.g. Nadiethyl-dithiocarbamate, tetraethyl-thiuramdisulfide, and di-(pentamethylene)-thiuramdisulfide) may be as active as Thiomycid (=Conteben). Less active than these compounds, but still of considerable activity are tetramethyl-thiuram-mono- and disulfide, tetra-ethyl- and di-(pentamethylene)-thiuram-monosulfide and N, N′-di-(4-ethoxyphenyl)-thiocarbamide.

"Fifty-eight compounds selected by *in vitro* testing were examined for their therapeutic effect in experimental guinea pig tuberculosis. The action of Thiomycid and of isonicotinic-acid-hydrazide was compared with the above compounds. Beside these two control substances only N, N′-(4-ethoxyphenyl)-thiocarbamide proved to have an *in vivo* activity. All other compounds had no effect at all.

"The consequences of these results are discussed."

See also p. 318, BHASKARAN, LAHIRI & GHOSE ROY, **Effect of Sewage Treatment Processes on Survival of Tubercle Bacilli.**

WILLIS, H. S., VANDIVIERE, H. M., VANDIVIERE, M. R. & MELVIN, Irene. **Studies in Tuberculo-Immunity.** *Amer. J. Med. Sci.* 1960, Aug., v. 240, No. 2, 137–28, 17 figs. [36 refs.]

In this study 4 strains of BCG were compared with the attenuated human strain R1 which had been maintained for 10 years by passaging in guineapigs, without culturing. The vaccines were produced by a standard procedure; after being grown twice for 8 days in Dubos medium the bacilli were grown in the same medium, but in which the bovine albumin had been replaced by human albumin, and then after 8 days' incubation the suspension was diluted to contain 1 mgm. viable bacilli

per ml. Viability was assessed by estimating the amount of formazan produced from 2,3,5-triphenyl tetrazolium chloride, a procedure which had been shown to correlate well with colony counts.

The potency of the 4 vaccines was then compared: (1) by the amount of Tween 80 necessary to prevent cord formation; (2) by the increase in weight of the omentum of guineapigs 14 days after intraperitoneal injection of 0·025 mgm. of living bacilli; (3) by the duration of allergy in guineapigs injected with 0·005 mgm. living bacilli and by the volume of the response to 1:1,000 OT; and (4) by the protection in vaccinated guineapigs, challenged with H37Rv, the assessment being made by the method of Feldman.

The results obtained by the 4 methods gave good agreement, the 3 strains of BCG showing marked differences in potency between themselves and all were inferior to R1. The degree of protection afforded by vaccination against H37Rv depended, however, on the size of the challenge dose; with a challenge dose of 9×10^5 bacilli, there was little protection by any of the vaccines and no quantitative difference between the vaccines could be detected when the challenge was 6 months after vaccination, although when the interval was increased to 12 months the R1 vaccine showed some superiority. The difference between the vaccines was shown most clearly when the challenge dose was reduced to about 3×10^4 bacilli, especially when the interval between vaccination and challenge was 18 to 30 months.

S. R. M. Bushby

KANAI, K. & YOUMANS, G. P. **Immunogenicity of Intracellular Particles and Cell Walls from *Mycobacterium tuberculosis*.** *J. Bacteriology*. 1960, Nov., v. 80, No. 5, 607–14, 4 figs. [23 refs.]

These intracellular particles, which may be mitochondria, have been shown to be immunogenic for mice [this *Bulletin*, 1958, v. 33, 511] and the cell walls have been reported to produce hypersensitivity of the delayed type in guineapigs [RIBI *et al.*, *ibid.*, 1176]; in the present paper these products obtained from disintegrated H37Ra and separated by differential centrifugation were injected intraperitoneally into mice and 1 week later the animals were challenged intravenously with H37Rv.

Judged by the number of mice that survived 30 days, the cell-wall fractions afforded some degree of protection, especially in the Strong A strain of mice, but this protection was less than that given by the intracellular particles in both the Strong A and CF-1 strains. The maximum effects obtained in the Strong A strain was 30% survival, by 10 mgm. of the cell wall and 62% survival by 10 mgm. of the particle fraction, these survival rates comparing with 11·6% of unvaccinated mice and 47·3% of mice vaccinated with 1·0 mgm. H37Ra. Heating the particle fractions for 30 minutes at 98°C. destroyed the immunogenicity of the particle fractions, but not that of the cellular wall.

In discussing these results, the authors consider the possibility of the activity of these particles depending upon maintenance of metabolic activity after introduction into the animal tissues.

S. R. M. Bushby

KANAI, K., YOUMANS, G. P. & YOUMANS, Anne S. **Allergenicity of Intracellular Particles, Cell Walls, and Cytoplasmic Fluid from *Mycobacterium tuberculosis*.** *J. Bacteriology*. 1960, Nov., v. 80, No. 5, 615–21. [14 refs.]

The authors describe experiments in which they tested the highly immunogenic particulate fraction and the poorly immunogenic cell-wall fraction of the previous paper [see above] for allergenicity and ability to elicit allergenic reactions in tuberculin-sensitive guineapigs; they also included in the experiments the soluble cytoplasmic fraction which consisted of proteins and carbohydrates.

Sensitization was attempted by: (1) one or two intraperitoneal injections of the fraction at weekly intervals, and cross-testing for sensitivity was made at 2·5–18 weeks later; and (2) intramuscular injection of a water-in-oil suspension of the antigens, and testing at 3, 6 and 9 weeks with tuberculin. H37Ra, which was included in the experiments as the control, and the cell-wall fraction induce a high state of tuberculin sensitivity, and only the animals sensitized with these two antigens developed delayed systemic fatal allergic reactions when injected intraperitoneally with 2 ml. of undiluted Old Tuberculin. However, all the fractions produced characteristic delayed type of of reaction of hypersensitivity when injected intradermally into guineapigs sensitized with the living intact bacilli or the cell walls. Treatment of the cell walls with alkaline ethanol at 37°C., but not with pepsin, trypsin or ribonuclease destroyed the allergenicity; the treatment with the ethanol presumably removed a lipoprotein moiety.

S. R. M. Bushby

BACKMAN, A. **The Influence of Induced Hyperthyroidism on Experimental Tuberculosis in Mice.** *Ann. Med. Exper. et Biol. Fenniae.* Helsinki. 1960, v. 38, Suppl. 3, 56 pp., 11 figs. [156 refs.]

MEISSNER, Gertrud. Atypische Mycobakterien. III. Mitteilung. Aviäre und avium-ähnliche Stämme. [**Atypical Mycobacteria. III. Avian and Avian-Like Strains**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 4, 510–21. [15 refs.]

The English summary appended to the paper is as follows:—

"No reliable cultural differences exist between Mycobacterium avium strains and strains similar to them. On the other hand, both groups can be differentiated by characteristic differences in their growth, temperature and their INH resistance, though exceptions from this rule may be found. Between both these groups differences of virulence may be present, but they are not always clear cut, since in the avian-like group strains of a high virulence as well as completely avirulent strains may occur.

"Such a variable symptom as the virulence should not be used for the differentiation of two subgroups within the large group III of the atypical Mycobacteria. It is proposed to omit the expression 'avium-like' and to use the term avian mycobacteria of low animal virulence."

BROCK, J. M., KENNEDY, C. B. & CLARK, W. H., Jr. **Cutaneous Infection with Atypical Mycobacterium. Report of a Case.** *Arch. Dermat.* 1960, Dec., v. 82, No. 6, 918–20, 3 figs.

"A case is reported of Group IV (Runyan) atypical mycobacterial infection of the thigh, which followed trauma and took the form of deep subcutaneous abscesses. The infection did not respond to isoniazid and streptomycin but cleared spontaneously within 26 months.

"Chronic subcutaneous abscesses or ulcerative granulomatous nodules, particularly on the extremities, may be caused by atypical Mycobacteria. If a specific culture for these organisms is done, the diagnosis can be made, but it will be missed if the physician does not carry the possibility in mind."

PARLETT, R. C. **A Modification of the Oakley Tube Method of the Agar Double-Diffusion Precipitation Test for Mycobacterial Antibodies.** *Internat. J. Leprosy.* Wash. 1960, July–Sept., v. 28, No. 3, 300–304.

NISHIMURA, S., KOSAKA, K. & YASUKAWA, T. **Immunological Relationship between Leprosy and Murine Leprosy. I. Antigenicity of Leprosy Bacillus and Murine Leprosy Bacillus in the Skin Reaction in Guinea Pigs.** *Biken's J.* Osaka. 1960, Aug., v. 3, No. 2, 173–82. [13 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1961, v. 58, 466.]

CHANG, Y. T. **Changes in the Length of *Mycobacterium leprae murium* in the Evolution of Murine Leprosy in Mice.** *Amer. Rev. Respiratory Dis.* 1960, Sept., v. 82, No. 3, 409–11, 2 figs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1961, v. 58, 327.]

KAGAN, G. I. & SAVENKOVA, V. T. **The Technique of obtaining L-Forms of *C. diphtheriae* and some Morphological Peculiarities.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 3, 449–53, 5 figs. [Translated from Russian.]

CRUZ, A. H., ELIAZO, E. E. & GOMEZ, Cecilia Z. ***Corynebacterium diphtheriae* in Skin Lesions.** *J. Philippine Med. Ass.* 1960, Oct., v. 36, No. 10, 755–6.

A report of 2 cases.

MASOUREDIS, S. P. **Behavior of intravenously administered I^{131} Diphtheria Toxoid in the Guinea Pig.** *J. Immunology.* 1960, Dec., v. 85, No. 6, 623–8, 2 figs. [14 refs.]

BRISOU, J., PELOUX, Y., CADEILLAN, J. & TYSSET, C. Bacille de Whitmore et *Flavobacterium* protéolytiques pathogènes. [**Whitmore's Bacillus and Pathogenic, Proteolytic *Flavobacterium***] *Bull. Soc. Path. Exot.* 1960, May–June, v. 53, No. 3, 435–43. [18 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1961, v. 58, 379.]

HOLLOWAY, B. W. **Grouping *Pseudomonas aeruginosa* by Lysogenicity and Pyocinogenicity.** *J. Path. & Bact.* 1960, Oct., v. 80, No. 2, 448–50.

"A method of grouping strains of *Pseudomonas aeruginosa* by using the characteristics of lysogenicity and pyocinogenicity is proposed. By this method 214 strains from various Melbourne hospitals have been placed into eighteen groups."

MARCUSE, K., HENZE, B. & POHLE, H. D. Das Vorkommen von Salmonellen in West-Berlin. II. Mitteilung. Epidemiologisch-soziologische Untersuchungen über das Vorkommen der Enteritis-Salmonellen in den Jahren 1955 bis 1957. [**Incidence of *Salmonella* in the City of West Berlin. II. 1955–1957**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 4, 478–92, 3 figs. [10 refs.]

PAPADAKIS, J. A. **Dulcitol-Sucrose-Salicin-Iron-Urea Agar (DSSIU)—a New Medium for Differential Diagnosis of Salmonellae.** *J. Hygiene.* 1960, Sept., v. 58, No. 3, 331–6, 2 figs. [13 refs.]

The essential feature of this medium is that it tests in a single tube culture the fermentation of 3 sugars, H_2S production and urea hydrolysis. The medium consists of two separate parts with different compositions, but with the same agar base. The part which is poured first to form the butt of the slope contains dulcitol and urea. When this is set the second part containing the iron, thiosulphate, urea, salicin and sucrose is poured and the tubes are sloped so that the previously poured medium is completely covered by the second medium as a slant. Both parts of the medium contain the same indicator which is a mixture of bromthymol blue and thymol blue as 0·2% solutions (each containing the appropriate amount of N/20 NaOH) in the proportion of 17 to 10 so that the uninoculated medium is dark green. The reactions which may be observed are: a yellow butt, sometimes containing gas bubbles indicates fermentation of dulcitol; blackening between slant and butt indicating H_2S production; a yellow slant means fermentation of sucrose or salicin while hydrolysis of urea produces a pure blue colour, usually throughout the medium. Some alkali-producing organisms give a greenish-blue colour to the slant.

Of 228 salmonella strains (56 serotypes), 204 gave typical salmonella reactions within 18 hours' incubation, while 6 others required 48 hours' incubation before showing typical reactions. There were, however, 18 strains whose reactions were still atypical after 48 hours' incubation.

[This might be considered to be a reasonably good differential medium for salmonellae for demonstration purposes, but whether a complicated medium of this sort has any real value as a time saver to the busy routine bacteriologist seems doubtful. Nevertheless it is an interesting piece of applied bacteriological technique.]

H. J. Bensted

PETERSEN, K. F. & ABU-GHAZALEH, R. Schnellmethode zur routinemässigen Prüfung der biochemischen Leistungen von Enterobakterien. [**A Rapid Method for Routine Testing of the Biochemical Properties of Enterobacteria**] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 146, No. 6, 510–21, 6 coloured figs. [21 refs.]

In 1949, KNOX [this *Bulletin*, 1950, v. 25, 623] described a screening plate for the rapid identification of faecal organisms. Of various later modifications of Knox's technique, the present authors chose that of SANDERS *et al.* [*ibid.*, 1957, v. 32, 986] as their starting point. The basic medium of the latter workers was inoculated with a suspension of the test organism and then paper discs impregnated with various sugars and other reagents placed on the surface of the medium. In the present study, an early finding was that if an extra layer of medium 1–2 mm. in thickness was superimposed on the inoculated plate, carbohydrate fermentation was demonstrable after only 30 minutes' incubation. Gas production could be read after 1–2 hours and H_2S production after 3–4 hours. The reactions were maximal after 8 hours and then became less distinct through increasing acidity of the entire plate but plates were readable for 36 hours if left on the bench after a preliminary 3-hour incubation.

A drawback to incorporation of iron ammonium sulphate in the original medium was that *Proteus* strains produced so much blackening that other reactions were masked. By sticking a lead acetate paper to the inner side of the Petri dish cover, weak H_2S production could be detected after 3 hours' incubation and strong production after 30 minutes. The lead acetate paper could also be applied as a disc on the surface of the medium.

Urease production could not be demonstrated on the original medium. By adjusting the final *p*H of the medium to 7·0, however, and incorporating thymol blue as well as phenol red, urease production was demonstrable within ½–1 hour. If overlooked after this time, the reaction tended to be masked by other changes in the medium.

The final medium recommended by the present authors contained casein peptone tryptic digest 10 gm., NaCl 5 gm., Bacto-agar 15 gm., phenol red 0·018 gm., thymol blue 0·018 gm., and distilled water 1 litre. After solution in the steamer, 0·6 gm. of sodium thiosulphate was added. The *p*H was adjusted to 7·0, the medium placed in a steamer and plates then poured. Each plate was inoculated with a fluid culture spread to give confluent growth, and after drying, the various impregnated discs were placed on the medium and covered with a second layer of medium as above described. Plates were then incubated at 37°C. for 3 hours and thereafter left on the bench at room temperature.

Using this method the authors tested 100 strains of faecal organisms for fermentation of glucose, lactose, sucrose, inosite, urease and H_2S production. All the results obtained tallied with those of tube tests on the same organisms.

In further work, the authors found that this plate method could also be used for the indole reaction. A disc impregnated with a solution containing dimethyl-p-aminobenzaldehyde 5 gm., methanol 50 ml. and phosphoric acid 10 ml. of concentrated solution was affixed to the Petri dish cover. The pink colour of a positive reaction could be read after 2–6 hours. *B. Moore*

RISCHE, H. & SCHNEIDER, H. Lysotypie und Transduktionsversuche mit einem laktose-positiven Typhus-Stamm. [**Phage-Typing and Transduction Experiments with a Lactose-Fermenting Typhoid Strain**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 179, No. 4, 522–7, 2 figs.

A lactose-fermenting but otherwise typical strain of *Salmonella typhi* phage type A was lysogenized with type-determining phage d 1 and changed into a lactose-fermenting type D 1 strain. Attempts to transduce the property of lactose fermentation from the latter strain to another non-lactose-fermenting phage type A culture were unsuccessful, although it was lysogenized with phage d 1 and became a non-lactose-fermenting phage type D 1 strain. *B. Moore*

OLÉS, A., STANIO, Barbara & SIKORSKA, Jadwiga. Die Resultate der Subtypisierung der Stämme *Salmonella typhi* von Lysotyp E_1 mittels des Bakteriophagen Vi VII (Brandis). [**The Results of Subtyping of the Strains *Salmonella typhi* of the Lysotype E_1 by means of the Bacteriophage Vi VII (Brandis)**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 3, 301–3.

The English summary appended to the paper is as follows:—

"258 strains of Salmonella typhi, originating from 65 foci of typhoid fever in the districts of Rzewsow and Lublin, were subtyped with the phage Vi VII. In 89% of the foci subtype E_{1A} was established."

PÖHN, H. P., RISCHE, H., BRANDIS, H. & SCHNEIDER, H. Zur Lysotypie von Typhus- und Paratyphus-B-Erregern in Deutschland in den Jahren 1953–1957. [**Phage Typing of Typhoid and Paratyphoid B Strains in Germany in the Years 1953–1957**] *Arch. f. Hyg. u. Bakt.* 1960, Oct., v. 144, No. 7, 505–18, 3 figs. [25 refs.]

This paper summarizes the phage typing experience of the Frankfurt and Wernigerode reference laboratories

during the years 1953–57. The strains examined came from all over East and West Germany apart from Bavaria, Schleswig-Holstein, Hamburg, Bremen and Berlin. The typhoid strains fell into 28 different phage types and are tabulated according to numbers of strains and numbers of individual epidemic foci concerned. In 67·7% of the foci investigated, one or other of 6 phage types was involved, *viz.* E 1, F 1, A, D 1, C 1 and D 2 in descending order of frequency. The results of ancillary typing methods for typhoid bacilli are also summarized, including the subdivision of phage type E 1 into sub-types a and b, the use of Nicolle's additional phages and the use of xylose fermentation as a differential character.

The strains of *Salmonella paratyphi B* fell into 10 different phage types, *viz.* 1, 2, 3a, 3aI, 3b, Jersey, Beccles, Taunton, BAOR and Dundee. Type Taunton was commonest and accounted for some 40% of foci in succeeding years. The Scholtens method of subdividing phage type Taunton was of no practical value because the Scholtens sub-type "Taunton—The Hague" was very rarely seen. Phage type 3aI was the next commonest with an incidence of about 13% of discrete foci and types 1 and BAOR each accounted for about 10–11%.

B. Moore

LENK, V., RASCH, K. & BULLING, E. Über das Vorkommen von *S. paratyphi* B (d-Tartrat negativ) bei Tieren. [**The Presence of *S. paratyphi* B (d-Tartrate Negative) in Animals**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 3, 304–9. [34 refs.]

The English summary appended to the paper is as follows:—

"Reports of salmonella paratyphi B in animals are rare and are received with reserve. In the present paper salmonella paratyphi B bacteria were demonstrated in a cow, which was almost certainly infected by a human carrier as yet unknown. Phage typing of the cultures isolated from human and cow uniformly yielded phage type '1 mc'. It is proposed in investigations in this manner always to make the differential diagnosis (d-tartrate-splitting and slime-wall formation) between salmonella paratyphi B and salmonella java."

KIRCHNER, C. E. J. **The Effects of the Mutator Gene on Molecular Changes and Mutation in *Salmonella typhimurium*.** *J. Molecular Biol.* London. 1960, Dec., v. 2, No. 6, 331–8. [14 refs.]

KERRIDGE, D. **The Effect of Inhibitors on the Formation of Flagella by *Salmonella typhimurium*.** *J. General Microbiol.* 1960, Dec., v. 23, No. 3, 519–38, 12 figs. [41 refs.]

MACKEL, D. C. & LANGLEY, Lorreine. **New *Salmonella* Type: Salmonella Phoenix.** *J. Bacteriology.* 1960, Dec., v. 80, No. 6, 863–4.

ŚLOPEK, S., MULCZYK, M. & GRZYBEK-HRYNCEWICZ, Kryspina. **Characteristic Features of a New Thermolabile Antigen of *S. flexneri* 1b.** *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1960, v. 8, No. 2, 191–201.

The thermolabile antigen described here differs from other thermolabile surface antigens found in members of the *Enterobacteriaceae* in that it possesses a greater resistance to high temperatures, alcohol and also to N HCl. Heating to 100°C. for 1, 2 or 2½ hours considerably reduces its agglutinability, its agglutinin binding capacity and its agglutinogenic power but unless suspensions of bacilli containing this antigen are heated to 120°C. for 2 hours these properties are not entirely destroyed. The authors found this antigen in a number of Flexner strains classified as 1b, but they also found related antigens in *Shigella flexneri* 1a, 2b, 3, 4 and Y type. It would appear, however, that the thermolabile antigen carried by these different Flexner types are not identical and it is suggested, at any rate as far as type 1b is concerned, that the antigen consists of 2 fractions, one of which is specific for 1b and the other which is shared by the types mentioned above.

[These observations are very similar to those made recently by IGNATOVA (this *Bulletin*, 1961, v. 36, 192). In neither case is it possible to exclude the presence of fimbrial antigens being responsible for the results observed (see DUGUID and GILLIES, this *Bulletin*, 1958, v. 33, 264).] *H. J. Bensted*

FRIEDMAN, H. & GABY, W. L. **Immunologic Unresponsiveness in Mice following Neonatal Exposure to *Shigella* Antigens.** *J. Immunology.* 1960, Nov., v. 85, No. 5, 478–82, 1 fig. [35 refs.]

The antigens used were saline suspensions of various concentrations of alcohol-killed *Shigella paradysenteriae* [presumably *Sh. flexneri*] and also a soluble derivative obtained by trypsinization of the cellular suspension. Newborn white mice were inoculated at various intervals after birth with 0·1 ml. of the various antigens injected subcutaneously, intramuscularly or intraperitoneally. At selected ages at maturity, groups of mice were challenged with an intramuscular injection of 0·1 ml. of a killed suspension of the same shigella strain containing 5×10^7 bacterial cells.

The neonatal injection of the relatively large doses of either the soluble or cellular shigella antigens induced a partial immunological unresponsiveness in these mice, but the effect was temporary and did not last longer than 5 weeks. The concentration of the antigen, route of inoculation and the age of the animal at the time of the primary inoculation were all factors which influenced the results. For instance, an intraperitoneal injection of the highest sublethal dose of antigen given within 24 hours of birth resulted in a 10-fold suppression (as compared with controls) in antibody response when the animals were challenged at 5 weeks of age.

Spleen cells, obtained from normal donor mice 5 weeks old that had been immunized 4 days previously with 0·1 ml. (10^8 cells) shigella vaccine, were transferred intraperitoneally into unresponsive mice of 5 weeks of age

and also into normal controls of the same age. Agglutinins appeared rapidly in both the control and the unresponsive mice, the antibody curves being almost identical. This reversal of the unresponsiveness by cold-washed suspensions of immune spleen cells was not seen with cell suspensions heated to 56°C. for 30 minutes. [See also FRIEDMAN and GABY, this *Bulletin*, 1960, v. 35, 1150.] *H. J. Bensted*

BEER, M., HIGHTON, P. J. & MCCARTHY, B. J. **Structure of Ribosomes from *Escherichia coli* as revealed by their Disintegration.** [Correspondence.] *J. Molecular Biol.* London. 1960, Dec., v. 2, No. 6, 447–9, 1 fig. & 1 pl.

VÁCZI, L., FODOR, M., RÉTHY, A. & HOLLÓS, I. **Studies on the Amino Acid Composition of the Cell Wall of *E. coli* 0:111 Strains with Different Antibiotic Sensitivity.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 3, 297–306, 4 figs. [17 refs.]

PONTIERI, G., SALVATORE, G., COVELLI, I. & ROCHE, J. Sur la présence chez *Escherichia coli* d'un système protéique fixant sélectivement les hormones thyroïdiennes. [**The Presence in *Escherichia coli* of a Protein System Selectively Fixing Thyroid Hormones**] *C.R. Soc. Biol.* 1960, v. 154, No. 7, 1369–74, 2 figs.

COVELLI, I. Sur l'affinité pour les iodothyronines des protéines endocellulaires d'*Escherichia coli*. [**The Affinity of Endocellular Proteins of *Escherichia coli* for Iodothyronines**] *C.R. Soc. Biol.* 1960, v. 154, No. 7, 1374–9, 2 figs.

ROGERS, D., KING, T. E. & CHELDELIN, V. H. **Glucosylglycine and Glycine Metabolism in *Escherichia coli*.** *J. Bacteriology.* 1960, Dec., v. 80, No. 6, 787–93, 3 figs. [14 refs.]

ROGERS, D. **Glucosylglycine, Asparagine, and Glutamine Metabolism in *Escherichia coli*.** *J. Bacteriology.* 1960, Dec., v. 80, No. 6, 794–800, 3 figs. and 1 diagram. [12 refs.]

KAISER, A. D. & HOGNESS, D. S. **The Transformation of *Escherichia coli* with Deoxyribonucleic Acid isolated from Bacteriophage *λdg*.** *J. Molecular Biol.* London. 1960, Dec., v. 2, No. 6, 392–415, 9 figs. and 1 pl. [48 refs.]

TAUSSIG, A. **The Effect of Carbamyl Phosphate and Cyanate of *Escherichia coli*.** *Canadian J. Microbiol.* Ottawa. 1960, Dec., v. 6, No. 6, 619–29, 5 figs. [11 refs.]

LOWE, G. H. **A Study of the Factors controlling Lactose-Fermentation in the Coliform and Paracolon Groups.** *J. General Microbiol.* 1960, Aug., v. 23, No. 1, 127–35, 1 fig. [10 refs.]

LE MINOR, L., EDWARDS, P. R. & FIFE, M. A. Quatre nouveaux sérotypes d'Arizona (1,4: 31: 30; 1,33: 23: 28; 9: 22: 21 et 9: 26: 30). [**Four New Arizona Serotypes, (1,4: 31: 30; 1,33: 23: 28; 9: 22: 21; and 9: 26: 30)**] *Ann. Inst. Pasteur.* 1961, Jan., v. 100, No. 1, 131–3.

REUSSE, U. Untersuchungen über die Leistungsfähigkeit der Nyiredy'schen Katalaseprobe für die Typendifferenzierung von Brucellen. [**Investigations on the Differentiation of *Brucella* types by Nyiredy's Method of Quantitative Catalase Determination**] Reprinted from *Monats. f. Tierheilk.* 1960, v. 12, No. 8, 125–8, 1 fig.

One ml. of a suitable diluted suspension of the *Brucella* and 5 ml. of 0·9% solution of H_2O_2 are mixed in a graduated tube and the amount of gas produced is read off. The yield with *Brucella suis* strains is on the average at least twice as great as with either *Brucella melitensis* or *Brucella abortus*.

This simple and direct method suffices for most strains; a few which give intermediate results should be more carefully titrated with permanganate following the method of HUDDLESON and STAHL (*Michigan State Tech. Bull.*, 1943, v. 182, 57). *J. W. McLeod*

URBASCHEK, B. Immunologische Studien an Brucellen. I. Chemische Fraktionierung von *Brucella abortus* Bang. [**Chemical Fractionation of *Brucella abortus* Bang**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Nov., v. 120, No. 4, 279–87. [27 refs.]

The English summary appended to the paper is as follows:—

"The pertinent literature is reviewed briefly. The biochemical separation of two lipo-polysaccharide fractions and a lipoid fraction with some subfractions is reported."

HEILMAN, Dorothy H., RICE, E., HOWARD, D. H., WEIMER, H. E. & CARPENTER, C. M. **Tissue Culture Studies on Bacterial Allergy in Experimental Brucellosis. II. The Cytotoxicity of Nucleoprotein Fractions of Brucellae.** *J. Immunology.* 1960, Sept., v. 85, No. 3, 258–67. [10 refs.]

In a previous paper HEILMAN *et al.* [this *Bulletin*, 1958, v. 33, 988] reported that a specific cytotoxic effect on cells from a sensitized host could be elicited with a whole cell brucella antigen. The present paper deals with the cytotoxic activity of Brucellergen (protein nucleate) and

similar nucleoprotein fractions prepared from *Brucella abortus, Br. melitensis* and *Br. suis*.

The specificity of the cytotoxic action of nucleoprotein fractions from *Brucella* species was tested in spleen explants from normal, brucella-infected and tuberculous guineapigs. The Brucellergen examined consisted of different batches of the commercial diagnostic product, but the nucleoprotein fractions of the 3 species of brucellae were specially prepared from smooth cultures of registered strains. Comparative potency tests of the preparations were determined by intracutaneous injections into the shaved skin on either side of the midline of the back of sensitized rabbits and the measurement of the skin reactions.

Cytotoxicity was determined by measuring the inhibition of migration and growth of macrophages, leucocytes and fibroblasts in the tissue cultures from the spleen explants. Morphological changes were studied in stained sections taken from the cultures after different periods of incubation.

At a dilution of 1:10 Brucellergen was non-toxic for the cells from normal animals, but it had a significant effect on the cells from brucella-sensitized guineapigs; the presence of brucella antibodies did not influence this effect. Purified protein derivative of tuberculin showed a similar effect on splenic cell cultures from tuberculous guineapigs but there was no evidence of crossing reactions; the Brucellergen and the PPD reactions were respectively specific. Each of the 3 nucleoprotein fractions when tested intradermally on a rabbit sensitized against *Br. melitensis* showed a delayed response and in splenic cell cultures, while the toxicity for normal cells was very low, the effect on the cells from brucella-infected animals was marked, but there was no evidence of species specificity. There was, however, some difference in the potency of the three nucleoprotein preparations; the splenic explants from guineapigs infected with *Br. suis* displayed a higher degree of sensitivity than the others and this may well be related to the severity of infections with this species in guineapigs. This difference is apparently due to some factor other than the nucleoprotein fraction. *H. J. Bensted*

SMITH, H.; KEPPIE, J.; COCKING, E. C.; WITT, K. **The Chemical Basis of the Virulence of *Pasteurella pestis*. I. The Isolation and the Aggressive Properties of *Past. pestis* and its Products from Infected Guinea-Pigs** [SMITH, KEPPIE, COCKING & WITT]. *Brit. J. Exper. Path.* 1960, Oct., v. 41, No. 5, 452–9, 1 fig. [24 refs.] **II. The Toxicity for Guinea-Pigs and Mice of Products of *Past. pestis*** [COCKING, KEPPIE, WITT & SMITH]. *Ibid.*, 460–71, 1 fig. [18 refs.] **III. An Immunogenic Product obtained from *Past. pestis* which protects both Guinea-Pigs and Mice** [KEPPIE, COCKING, WITT & SMITH]. *Ibid.* 1960, Dec., v. 41, No. 6, 577–85, 1 fig. on pl. [14 refs.]

[An abstract of these papers appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 448.]

DODIN, A. & BRYGOO, E. R. Activité succinodéshydrogénasique de *Pasteurella pestis*, souche E.V. II. Étude manométrique. [**Succinodehydrogenase Activity of *Pasteurella pestis* Strain EV. II. Manometric Study**] *Arch. Inst. Pasteur de Madagascar.* 1960, v. 28, 17–18.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 313.]

ROTH, I. L., LEWIS, C. W., Jr. & WILLIAMS, R. P. **Electron Microscope Study of *Bacillus anthracis* in Mouse Spleen.** *J. Bacteriology.* 1960, Dec., v. 80, No. 6, 772–82, 7 figs. [20 refs.]

BOSCO, G. Sulla capacità di sopravvivenza delle spore. [**The Survival Capacity of Spores**] *Nuovi Ann. d'Igiene e Microbiol.* 1960, July–Aug., v. 11, No. 4, 335–8. [64 refs.]

The English summary appended to the paper is as follows:—

"Some longevity records concerning bacterial spores preserved in sealed vials and test tubes are here reported. Spores of *B. anthracis* were viable after 47, 46 and 23 years. Spores of *Cl. tetani* were found alive after 34 years."

TOMCSIK, J. & BOUILLE, M. Effets cytologiques des enzymes produites au cours de la sporulation des bacilles aérobies. [**Cytological Effects of Enzymes elaborated in the Course of Sporulation of Aerobic Bacilli**] *Ann. Inst. Pasteur.* 1961, Jan., v. 100, No. 1, 25–36, 8 figs. on 2 pls. [19 refs.]

The English summary appended to the paper is as follows:—

"The elaboration of V-enzymes, isolated for the first time by Strange and Dark, is with very few exceptions strictly parallel to the sporulation of *B. cereus* and *B. anthracis*. Their cytological effect at pH 4·6 is before all a cell-wall lysis: bacterial chains are sectioned by lysis of transversal cell-walls, then granular disintegration followed by dissolution of lateral cell-walls takes place. The effect of these enzymes is delayed or inhibited by cell-wall anti-polysaccharide antibodies, whereas anti-polypeptide antibodies have almost no influence.

"The cytoplasmolytic effect of V-enzymes is negligible. The cytoplasm released by disintegration of the cell-walls is dissolved in isotonic sucrose solution, Ringer or saline solutions.

"Certain sera protect the cytoplasmic elements, which then take a spherical form and differ from *B. megaterium* protoplasts induced by lysozyme."

COLOBERT, L. De la nature de la membrane limitant les protoplastes obtenus par l'action du lysozyme sur *Bacillus megaterium*. [**Nature of the Membrane limiting the Protoplasts obtained by Action of Lysozyme on *Bacillus megaterium***] *Ann. Inst. Pasteur.* 1961, Jan., v. 100, No. 1, 37–52, 5 figs. [30 refs.]

WILLIS, A. T. **The Lipolytic Activity of Some Clostridia.** *J. Path. & Bact.* 1960, Oct., v. 80, No. 2, 379–90, 16 figs. [15 (6 coloured) on 4 pls.] [26 refs.]

By using media containing various fats, tributyrin, cream, egg-yolk and lecithin nutrient agars for the growth of *Clostridium oedematiens* type A, *Cl. sporogenes* and *Cl. botulinum* type A-E, results were obtained which support and extend earlier work (Willis, *Nature*, 1960, v. 185, 943) that both the pearly layers and the associated opalescence by these organisms on fat-containing media is often due to lipolytic activity releasing free fatty acid. The layers stained bright greenish-blue with copper sulphate. Changes did not occur on fat-free nutrient agar and milk agar. *Cl. welchii, Cl. bifermentans, Cl. sordellii* and *Cl. oedematiens* type B did not give lipolytic reactions, although they produced a diffuse opalescence on egg-yolk agar from lecithinase C activity.

Betty C. Hobbs

D'ARCA SIMONETTI, A. Sull'emolisina della tossina botulinica E. **[The Haemolytic Fraction of Botulinus E Toxin]** *Nuovi Ann. d'Igiene e Microbiol.* 1960, July-Aug., v. 11, No. 4, 295–300.

The English summary appended to the paper is as follows:—

"The haemolytic fraction of botulinus E toxin has been studied with particular reference to:

"*a*) its behaviour at various temperatures and in various conditions of aerobiosis and anaerobiosis;

"*b*) its behaviour in contact with various oxidizing and reducing agents;

"*c*) the influence exercised upon it by the five anti-botulinus immune sera A B C D E, by antiperfringens serum, by antitetanus serum and by normal human serum.

"The investigations have led to the conclusion that botulinus toxin E has a thermolabile haemolytic component (completely inactivated after 24h at 37°C) which is oxidized in the presence of air (after 10 days at 20°C. in aerobic conditions it loses 70% of its activity, while after 10 days at the same temperature but in conditions of semianaerobiosis activity is reduced only by 25%), and neutralized by normal human as well as by all the immune sera examined (antibotulinus A B C D E, antiperfringens, antitetanus)."

PARNAS, J., KOSLAK, A. & KRUKOWSKA, Maria. Untersuchungen der Leptospirenlipase. **[Studies on Leptospiral Lipase]** *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 3, 386–9.

An English version of the author's summary is as follows:—

"(a) Lipase activity was found in the following strains: L. javanica, L. poi, L. sarmin, L. ballum, L. autumnalis AB, L. grippotyphosa Bernkopf, L. hardje, L. sejroe, L. saxkoebing, L. hyos.

"(b) No lipase activity was detected in: L. icterohaemorrhagiae AB, L. icterohaemorrhagiae A, L. mankarse, L. schüffneri, L. canicola, L. benjamin, L. pyrogenes, L. australis B, L. cynopteri, L. sentot, L. bangkinang, L. autumnalis A, L. djasiman, L. australis A, L. muenchen, L. pomona, L. grippotyphosa Moscow V and Duyster, L. hebdomadis, L. medanensis, L. wolffi, L. bataviae, L. paidjan, L. semarang."

(i) LABZOFFSKY, N. A. & KELEN, A. E. **Studies on Complement Fixing Antigens of Leptospirae.** *Canadian J. Microbiol.* Ottawa. 1960, Aug., v. 6, No. 4, 453–62, 2 figs.

(ii) KELEN, A. E. & LABZOFFSKY, N. A. **Studies on Latex Agglutination Test for Leptospirosis.** *Ibid.*, 463–73, 2 figs. on 2 pls. [11 refs.]

(i) Complement fixation has not been generally accepted as the method of choice in the sero-diagnosis of leptospirosis owing, probably, to the lack of a simple and reliable procedure for preparing satisfactory antigen. Of the antigens so far reported the authors prefer those of TERZIN [this *Bulletin*, 1957, v. 32, 502]. The present report deals with 2 new antigens which were prepared from cultures of *Leptospira icterohaemorrhagiae, L. canicola,* and *L. pomona.* These antigens are stable, withstanding boiling for 10 minutes and storage for at least 2 months at 4°C., and they are free of anticomplementary properties, even in low dilutions. Moreover, they are soluble in the true sense since they are not sedimented at 40,000 r.p.m. and are filterable through ultra-fine fritted glass.

"Whole" antigen is prepared by adding pyridine to cultures 3–4 weeks old. The resulting precipitate is removed by centrifugation. The supernatant fluid is dialyzed and concentrated by pervaporation, then centrifuged. The final supernatant fluid is "whole" antigen. Type-specific antigen is prepared from "whole" antigen by centrifugation at 40,000 r.p.m. followed by filtration through ultra-fine fritted glass filters; acetone is added to the filtrate and the resulting precipitate is dried, then reconstituted with distilled water to about 1/10 the original volume. The yield is small.

Type-specific antigens reacted only with the homologous antisera. There was considerable cross-reaction between "whole" antigens and the respective rabbit hyperimmune sera. Thus "whole" antigen tends to be group-specific; but titres with homologous sera were always higher. Cross-reactions were not so pronounced with sera from 28 cattle naturally infected with *L. pomona*: 12 reacted only with *pomona* antigen. These antigens were apparently rather more sensitive than those of Terzin.

On testing the sera of infected rabbits with the "whole" antigens, it was found that homologous antibody was detectable on the 4th day of infection and persisted for about 24 weeks, whereas heterologous antibodies appeared about the 7th day and disappeared earlier.

In view of the dominance and persistence of homologous antibodies, the authors conclude that a polyvalent antigen is necessary for routine screening tests.

"Whole" antigens are suitable for preparing a suitable polyvalent antigen.

(ii) Recent investigations have shown that latex particles can be successfully used in agglutination tests for various antigen-antibody reactions. MURASCHI recently reported the use of formalinized leptospires as antigen in such a test [this *Bulletin*, 1960 v. 35, 1008]. However, according to SINGER and PLOTZ (*Amer. J. Med.*, 1956, v. 21, 888) who developed the latex-fixation technique, the reaction is probably one between *soluble* antigens (coated on the surface of the latex particles) and the corresponding antibodies which is then manifested by aggregation of the particles. The authors therefore investigated the applicability of their soluble "whole" antigens to a latex agglutination test (LAT).

Stock latex suspension was prepared from a commercial preparation, of polystyrene particles 0·81μ in diameter, which was diluted 1:2·5 with distilled water, filtered through Whatman No. 4 paper and stored at 4°C. "Final" latex suspension was prepared by diluting the stock suspension with borate-buffered saline, *p*H 8·2, to give a 0·6% suspension (this corresponded to an optical density of 0·30 as determined by the Coleman Nepho-colorimeter at a wave-length of 665 mμ).

Test antigens were prepared by mixing 1 part of undiluted "whole" antigen with 19 parts of "final" latex suspension. After overnight adsorption at room temperature, this test antigen was stored, until used, at 4°C., at which temperature it is stable for at least 9 months.

The test is performed by adding 0·5 ml. amounts of antigen to 0·5 ml. volumes of 2-fold serial dilutions of serum and incubating for 2 hours at 37°C. The results are read with the naked eye after centrifugation at 2,000 r.p.m. for 5 minutes, or by low-power microscopy of drops from each tube without previous centrifugation to throw down the particles.

Evaluation of this latex-agglutination test (LAT) indicated that it has a high degree of specificity and a sensitivity intermediate between that of macroscopic agglutination and complement-fixation tests. The authors claim the following advantages for the LAT: simple and rapid performance; and the use of stable antigens, which eliminates the necessity of maintaining live leptospiral cultures in diagnostic laboratories. *L. H. Turner*

LINSCOTT, W. D. & BOAK, Ruth A. **Protective Action of Glycerol in the freezing of Leptospirae.** *J. Bacteriology.* 1960, Oct., v. 80, No. 4, 573–4.

The authors demonstrated that 2·5% glycerol exerted a marked protective effect on several (but not all) strains of leptospires investigated when it was added to cultures which were then frozen slowly in a −25°C. refrigerator; but 1% glycerol was much less effective. Under similar circumstances, 5·0% glycerol had much the same effect as the 2·5% concentration; but when cultures were frozen rapidly (by immersion in dry ice and ethyl alcohol) the protection afforded was negligible.

Long-term storage was not attempted. In this study the cultures were thawed after 2 days; they were then examined for motility, and subcultures were made (which were successful if more than 0·5% of leptospires were motile).

The authors suggest that cultures of leptospires protected by glycerol should be kept at −70°C. or lower (in sealed glass tubes to exclude CO_2 which is toxic to leptospires). [WOLFF, (this *Bulletin*, 1955, v. 30, 86) stated that all the cultures which were kept in his laboratory at −70°C. could be transferred successfully 1 and even 3 years after being frozen.] *L. H. Turner*

ADDAMIANO, L., BABUDIERI, B. & SMITH, J. W. Zwei neue zur Gruppe *Leptospira canicola* gehörige Serotypen. [**Two New Serotypes of the *Leptospira canicola* Group**] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 3, 419–21.

The English summary appended to the paper is as follows:—

"Two new Leptospira serotypes: L. bindjei and L. broomi, belonging to the 'canicola' serogroup, are described."

PARNAS, J., KOSLAK, A. & KRUKOWSKA, Maria. *Leptospira bataviae* in eigenen Untersuchungen. [**Investigations of *Leptospira bataviae***] *Zent. f. Bakt.* I. Abt. Orig. 1960, v. 180, No. 3, 379–86, 3 figs.

The English summary appended to the paper is as follows:—

"4,327 small mammals were investigated for Leptospirosis using serological, bacteriological and histological methods. The following results were obtained:

"a) In 10 animals the blood serum agglutinated only *Leptospira bataviae* with titres from 1:80 to 1:1280.

"b) In 13 animals mixed leptospiral infections could be traced, since the sera agglutinated not only *Leptospira bataviae* with titres from 1:80 to 1:320 but also other serotypes of Leptospirae.

"c) Three strains of *Leptospira bataviae* could be isolated from *Microtus arvalis*, *Mus musculus* and *Erinaceus roumanicus*.

"d) Histological examinations of 23 small mammals yielded no pathological findings."

WOLFF, J. W. & BOHLANDER, H. J. **Serological Classification of Five Strains of Leptospires belonging to the *Hyos* Serogroup.** *Trop. & Geograph. Med.* Amsterdam. 1960, June, v. 12, No. 2, 173–9. [21 refs.]

In 1942 Johnson isolated a strain of *Leptospira*, from a human patient in Australia, which he named *L. mitis*. In 1944, a similar serotype, isolated from pigs in Argentina, was named *L. hyos*. [The specific epithet, *mitis* had been effectively published in 1938 to designate strains which proved to be identical with *L. bataviae*; *L. hyos* is therefore the correct designation.] In 1938 a similar strain was isolated in the U.S.S.R.; but no report was published. Strains belonging to this Hyos serogroup have now been isolated in many parts of the world, mainly from pigs and human patients but also from rats (Malaya) and opossums (Georgia, U.S.A.).

Strains belonging to the Hyos serogroup give very little reaction, in agglutination tests, with other leptospires except with strains of the Bataviae serogroup and then only to a low titre (about 0·3–1·0%).

Antigenic differences between members of the Hyos serogroup do occur, as reported in the present paper. However, the suggestion that strain *hyos* is the "complete" biotype, and strain *mitis* (Johnson) the "incomplete" one, is based on differences well below the recommended limits [this *Bulletin*, 1954, v. 29, 877].

The authors subjected 5 strains to serological analysis: RP-29, one of 3 strains isolated from the kidneys of normal pigs in Brazil [*ibid.*, 1949, v. 24, 759]; Kisuba, one of several strains isolated from human patients in eastern Belgian Congo [*ibid.*, 1956, v. 31, 909]; and LT-79, LT-81, and LT-82, all isolated from the kidneys of opossums trapped in Georgia, U.S.A. The results of agglutination reactions and cross-absorption tests with these 5 strains, and with strains *hyos* and *mitis* Johnson, are tabulated. In view of their findings, the authors propose the following classification of the Hyos serogroup:

Serotype:	sub-serotype:	Type Strain:
hyos	*hyos*	mitis Johnson
hyos	*guidae*	RP-29
hyos	*bakeri*	LT-79
kisuba		Kisuba
atlantae		LT-81

Strain LT-82 was identical with LT-81.

L. H. Turner

GALTON, Mildred M., GORMAN, G. W. & SHOTTS, E. B., Jr. **A New Leptospiral Subserotype in the Hebdomadis Group.** *Pub. Health Rep.* Wash. 1960, Oct., v. 75, No. 10, 917–21. [18 refs.]

Investigations of the possible wild animal reservoirs of leptospires were made by the staff of the Communicable Disease Center (Chamblee) in Georgia, U.S.A., between 1953 and 1958. Leptospires were isolated, by direct culture of kidney tissue, from 15 racoons (*Procyon lotor*), 4 opossums (*Didelphis marsupialis*), and 1 striped skunk (*Mephitis mephitis*) which were trapped in the south-western part of Georgia which lies between the Flint and Chattahoochee Rivers.

The 20 isolated strains appeared to be identical and to belong to the Hebdomadis serogroup. Antigenic analysis, reported in this paper, indicates that these strains constitute a new subserotype of *Leptospira mini*; and the authors propose the designation *Leptospira mini georgia*.

Since 1952 serological evidence in cattle of infections with members of the Hebdomadis serogroup has often been observed. In 1952 GALTON *et al.* found agglutinins to *L. sejroe* (*J. Amer. Vet. Med. Ass.*, 1956, v. 128, 87) but their significance has not been fully determined. Meanwhile, ROTH and GALTON (*Amer. J. Vet. Res.*, 1960, v. 21, 422) have isolated another related serotype, *L. hardjo*, from cattle in Louisiana. The possible involvement of *L. mini georgia* in leptospirosis of cattle should now be considered.

The serum of some of the animals (notably racoons) from which *L. mini georgia* was isolated failed to agglutinate this organism, and a few reacted only very weakly with other strains of *L. mini*. A similar situation, in respect of small rodents infected with *L. ballum* or a member of the Hebdomadis serogroup, was recently reported by BROOM and COGHLAN [this *Bulletin*, 1960, v. 35, 1139]. Serological surveys of wild animals may therefore be misleading, and parallel kidney cultures should always be attempted.

Suggestive serological evidence of infection with *L. mini georgia* in a woman is briefly reported [and a fully documented case is also recorded by GOLEY *et al.*, p. 369].

L. H. Turner

FÜZI, M. & CSÓKA, R. **Antigenic Relationships among *Leptospira leeds* and Water Leptospirae.** *J. Bacteriology.* 1960, Oct., v. 80, No. 4, 569.

The Leeds strain of *Leptospira* was isolated from the urine and vesical mucosa of a patient with abacterial cystitis by CZEKALOWSKI and HORNE [*Brit. Med. J.*, 1951, ii, 879]. A more detailed description of the strain [this *Bulletin*, 1954, v. 29, 880] indicated that it was not related antigenically to some of the pathogenic serotypes common in Europe, or to a strain of the saprophytic water leptospire, *L. biflexa*. Füzi and Csóka found that the Leeds strain bore no antigenic relationship to 52 strains of pathogenic leptospires representing all the currently recognized serotypes; moreover, the strain was non-pathogenic in laboratory animals, and it had biological properties similar to those of water leptospires.

The authors now report their results of an investigation into the cross-reactions of 12 strains of *L. biflexa* with 3 anti-Leeds hyperimmune rabbit sera, the homologous titres of which were 12,800 (2 sera) and 25,600. The corresponding titres with *L. biflexa* AM 20 were the highest: 800 with 2 of the sera, and 3,200 with the other. Weaker reactions were observed with 4 other strains. Saprophytic leptospires give only occasional low-titre cross-reactions with antisera against pathogenic strains, but regularly cross-react with antisera against several saprophytic strains. The authors therefore consider that their latest results are further proof that the Leeds strain should be classified with the *L. biflexa* group.

L. H. Turner

PATOCKA, F., MÁRA, M. & SCHINDLER, J. **Pyridoxine as an Essential Growth Factor of *Listeria monocytogenes*.** *J. Hyg., Epidemiol., Microbiol. & Immunol.* Prague. 1960, v. 4, No. 4, 504–8, 2 figs.

"1. The authors studied growth of 38 strains of *Listeria monocytogenes* of human origin on a semi-defined medium containing glucose, inorganic salts and vitamin-free casein hydrolysate, with special reference to the influence of the vitamin B group.

"2. The only vitamin which stimulated growth alone on this medium was riboflavin. Biotin stimulated growth only in the presence of riboflavin.

"3. Another growth factor, which can be substituted for biotin, is pyridoxine. Like biotin, it is effective only in the presence of riboflavin.

"4. The influence of thiamine on growth of *Listeria monocytogenes* was not demonstrated.

"5. No differences in relative values were observed between the individual strains."

PANT, K. D.; SHRIVASTAVA, D. L.; MISRA, S. B. **Studies in Immunochemistry of *Vibrio cholerae*. Part II. Preparation of Polysaccharides from Growth on Agar** [PANT & SHRIVASTAVA]. *Indian J. Med. Res.* 1960, Nov., v. 48, No. 6, 677–82, 1 fig. & 1 graph. [14 refs.] **Part III. Characterization of Polysaccharides isolated from Broth Cultures** [MISRA & SHRIVASTAVA]. *Ibid.*, 683–91, 1 fig. & 1 graph. [20 refs.]

GHOSH, D. K., HALDAR, D., GHOSH, B. K. & CHATTERJEE, A. N. **Pentose Phosphate Cycle in *Vibrio cholerae*.** *Ann. Biochem. & Exper. Med.* Calcutta. 1960, Aug., v. 20, No. 8, 221–6, 3 figs. [12 refs.]

HOWARD, Mary B. & LANKFORD, C. E. **Minimum Nutritional Requirements for Mucinase Synthesis by *Vibrio cholerae*.** *Texas Reports on Biol. & Med.* 1960, v. 18, No. 4, 612–19. [15 refs.]

BACTERIOPHAGES

KANTOCH, M. & SZALATY, Helena. **Lytic Activity of Bacteriophages toward Phagocytized Bacteria.** *Archiwum Immunol. i Terapii Dośw.* Warsaw. 1960, v. 8, No. 3, 407–16, 1 fig. [14 refs.]

Guineapig leucocytes were mixed with *Escherichia coli* B cells to which T5 phage had been adsorbed and the phagocytic index was measured at intervals. During the first 20 minutes it rose as much as in controls put up with bacteria to which heat-inactivated phage had been adsorbed. When the end of the latent period of the phage was due, the phagocytic index fell in the experimental tubes while remaining constant in the control tubes. When T2 or T5 phage was added to a suspension of leucocytes containing bacteria at a time when the phagocytic index was maximal, the results were no different from the controls.

It is concluded that phage-infected bacteria go on to lyse within the leucocyte but that phage cannot penetrate the leucocyte to infect bacteria already engulfed.

Janice Taverne

OTSUJI, N. & OKUBO, S. **Reactivation of Ultraviolet- and Nitrous Acid-Inactivated Phages by Host Cells.** *Virology.* New York. 1960, Dec., v. 12, No. 4, 607–9, 2 figs.

SAUERBIER, W. **Reaction of Formaldehyde with Deoxyribonucleic Acid in Phage *T1*.** [Correspondence.] *Nature.* 1960, Oct. 22, v. 188, 327–9, 2 figs.

Theoretically, inactivation of T1 by formaldehyde could result from damage to protein or to phage DNA. To find out what sort of damage has in fact occurred, the action of formaldehyde on T1 has been compared with that of UV light, an agent which is known to damage the phage genome without interfering with phage adsorption or injection of DNA. A proportion of the genetic damage caused by UV irradiation can be reactivated by the host cell, it is thought by recombination with bacterial genetic material [TESSMAN, *Virology*, 1956, v. 2, 679; this *Bulletin*, 1957, v. 32, (275)], and this reactivation, which necessarily indicates that penetration of phage DNA has occurred, can be prevented by allowing inactivated phage particles to adsorb to *Escherichia coli* B cells which have previously been exposed to UV irradiation.

Inactivation of T1 by formaldehyde in distilled water at *p*H 5·6 was an exponential function of formaldehyde dose. Fewer phage particles were recovered after adsorption of inactivated phage to irradiated than to unirradiated bacteria. Thus, it is argued, reactivation by the host cell had taken place and injection of phage DNA had not therefore been prevented by formaldehyde treatment. The proportion of the total inactivation which could not be reactivated was the same for formaldehyde as for UV irradiation. Further experiments on the effect of UV irradiation on phage inactivated by formaldehyde also suggested that inactivation of T1 by formaldehyde is mainly caused by reaction with the phage genome.

Formaldehyde is known to bind RNA by reacting with amino groups of the bases. It is not supposed to react with amino groups involved in hydrogen bondings, as is the case in double-stranded DNA (STAEHELIN, *Biochim. et Biophys. Acta.*, 1958, v. 29, 410). It is concluded therefore that some amino groups in the DNA of phage T1 must be free and that not all possible hydrogen bonds are established. *Janice Taverne*

SAUERBIER, W. **Effects of Ultra-Violet Light on Hydrogen Bonds in Deoxyribonucleic Acid of Phage *T1*.** [Correspondence.] *Nature.* 1960, Oct. 22, v. 188, 329–30, 3 figs.

If UV light breaks hydrogen bonds in double-stranded DNA, then irradiation of phage T1 should increase its sensitivity to formaldehyde [see above]. It was found that T1 was inactivated much faster if formaldehyde was

present during UV irradiation than if the phage was first treated with formaldehyde and the formaldehyde removed before irradiation. Formaldehyde inactivation was greater with increasing UV dose. This suggested that more amino groups became free to react after hydrogen bonds were broken by UV, and that the breaks themselves did not inactivate the phage. The breakage of the bonds was not reversed immediately as the phage showed an increased sensitivity to formaldehyde for at least 24 hours after irradiation.

In contrast, the rate of inactivation by UV light of ϕX 174, a phage known to contain single-stranded DNA, was not increased when formaldehyde was present during irradiation. This experiment also showed that, for ϕX 174 at least, any reaction of formaldehyde with protein did not cause inactivation of the phage.

Janice Taverne

MERCER, C. K. & MILLS, R. F. N. **Interference with Multiplication of Pc Phage by a Factor produced by Exposure of *Pseudomonas aeruginosa* to Inactivated Pc Phage.** *J. General Microbiol.* 1960, Oct., v. 23, No. 2, 253–6.

The authors report the production of a substance in some ways resembling interferon by bacteria which have been treated with inactive phage. A culture of *Pseudomonas aeruginosa* [*pyocyanea*] strain C 10 incubated for 2 hours at 37°C. with phage Pc which had been inactivated by acid or heat produced a substance which depressed the yield of phage Pc from a single cycle of infection. The substance was present in culture fluids, but disrupted cells were found to have greater activity. The substance did not inactivate free phage. It only depressed phage yield when added to bacteria before infection, the yield being least when it was added 1 hour before infection. It had less effect if it was removed after the adsorption period than if it was present throughout the phage growth cycle. The substance also interfered with the synthesis by *Ps. pyocyanea* of the serologically unrelated phage Pa, but did not affect the multiplication of Newcastle disease virus in tissue culture.

The phage inhibitory factor thus resembled interferon in being produced by host cells in response to inactive virus, in not affecting free virus, and in needing time to exert its full effect. However, it was more resistant to heat than interferon and did not pass into the culture medium as readily. *Janice Taverne*

VIRUSES

The order in this section is:—**General; Psittacosis-Lymphogranuloma group; Pox group; Respiratory group; Reovirus group; Enteric group; Arthropod-borne group; Others.**

MAGRASSI, F., ALTUCCI, P., BUONANNO, G. A., LORENZUTTI, G., SAPIO, U., CAVALLINI, G. & MASSARANI, E. Identificazione di farmaci (derivati chetoaldeidici del difenile) attivi nele infezioni da virus epatitici del topo. **[The Identification of Compounds (Keto-aldehyde Derivatives of Biphenyl) with Activity against Mouse Hepatitis Virus Infection]** *Giorn. di Malattie Infettive e Parassit.* 1960, Mar.–Apr., v. 12, Nos. 3/4, 119–30. [12 refs.]

The authors have studied the activity of 3 keto-aldehyde derivatives of biphenyl (bisulphite compound of 5-biphenylylglyoxal, 3′-chloro-4′-methoxy-4-biphenylylglyoxal hydrate and 4:4′-*bis*-biphenylylglyoxal hydrate) in mice infected with mouse hepatitis virus. The compounds were administered for periods up to 11 days in doses ranging from 3·35 to 1,000 mgm. per kgm. The results are presented in detail in tables. An increase in the percentage survival was noted in most cases. Animals which survived after treatment were immune to reinfection with the same virus. *D. J. Bauer*

MAGRASSI, F., ALTUCCI, P., BUONANNO, G. A., BUONINCONTI, R., DI SIMONE, A., LORENZUTTI, G., PECORI, V. & SAPIO, U. Applicazioni in campo umano della Xenalamina, farmaco di sintesi (derivato chetoaldeidico del difenile) ad attività protettiva in diverse infezioni da virus. II. Sua attività chemioterapica nell'infezione umana da virus influenzale. **[The Use in Man of Xenalamine, a Synthetic Drug (a Keto-Aldehyde Derivative of Biphenyl) with Protective Activity in Various Virus Infections. II. Its Chemotherapeutic Activity in Human Influenza Infection]** *Giorn. di Malattie Infettive e Parassit.* 1960, Mar.–Apr., v. 12, Nos. 3/4, 131–42, 15 graphs. [12 refs.]

The authors have carried out clinical trials of Xenalamine (a keto-aldehyde derivative of biphenyl) in influenza. The compound was given [presumably by mouth] in doses of 2–2½ gm. per day for 4–7 days to 228 patients suffering from Asian or type B influenza, and 206 similar patients treated symptomatically were observed as controls. The results are presented in great detail in tables and figures, and show in general that the treatment caused some reduction in the febrile period and duration of illness. *D. J. Bauer*

COLTORTI, M., ALTUCCI, P., BUONANNO, G. A., LORENZUTTI, G., PIAZZA, M. & SAPIO, U. Andamento di alcune variazioni biochimiche a livello del fegato e del plasma nell'infezione di MHV-3 Craig sotto l'influenza di trattamento chemioterapico con un derivato chetoaldeidico del difenile. [**The Course of Certain Biochemical Changes in the Liver and the Plasma in Infection with MHV-3 Virus under the Influence of Chemotherapeutic Treatment with a Keto-aldehyde Derivative of Biphenyl**] *Giorn. di Malattie Infettive e Parassit.* 1960, Mar.–Apr., v. 12, Nos. 3–4, 142–6, 1 chart. [12 refs.]

Mice were infected with the MHV-3 strain of mouse hepatitis virus and treated with 4:4′-*bis*-biphenylylglyoxal in a dose of 170 mgm./kgm., given 24 hours before infection and continued each day up to 10 days after infection. Determinations of the serum transaminase activity carried out at intervals after infection gave lower values than those obtained in control experiments with similarly infected mice which were not treated with the compound. A similar effect was observed in determinations of the oxidative phosphorylation of homogenates of the liver. The results are interpreted as indicating that the severity of the virus infection of the liver is modified by treatment with the compound.

D. J. Bauer

PUMPER, R. W. & YAMASHIROYA, H. M. **The Isolation and Virus Cytopathogenicity of a Line of Cells from Human Keratoacanthoma.** *Amer. J. Hyg.* 1960, Nov., v. 72, No. 3, 284–8, 4 figs. on pl. [20 refs.]

"A line of cells, isolated from human keratoacanthoma tissue, has been grown continuously in vitro for 6 months. The cells were isolated and are propagated on a simple medium consisting of 20 per cent horse serum and 80 per cent medium no. 199. These cells show a cytopathic response to poliomyelitis types 1, 2, 3, influenza A (PR8), B (Lee and B54) and vaccinia (IHD-E). Hemadsorption tests carried out in the case of influenza viruses were positive. The significance of the keratoacanthoma tissue isolation and future virus experiments are discussed."

SIMON, M. & JANCSÓ, Agnes. **The Virus Spectrum of a Cell Line derived from Monkey Kidney Cells.** *Acta Microbiologica.* Budapest. 1960, v. 7, No. 3, 215–23, 4 figs. [10 refs.]

ZÁVADA, J., KRIZANOVÁ, O. & BORECKÝ, L. **A Factor destroying Virus Receptors in Pneumococcal Cultures. IV. The Concentration and Partial Purification of Pneumococcal Factor 103 (Pn-f-103) and Differentiation from RDE of *Vibrio cholerae*.** *Acta Virologica.* Prague. 1961, Jan., v. 5, No. 1, 59–60.

POLLARD, M., STARR, T. J., MOORE, R. W. & TANAMI, Y. **Cytochemical Changes in Human Amnion Cells infected with Psittacosis Virus.** [Correspondence.] *Nature.* 1960, Nov. 26, v. 188, 770.

Using fluorescent microscopy after acridine orange staining and Feulgen's method of staining, the authors have followed the development of psittacosis virus when growing in human amnion cell cultures. DNA (yellow-green) particles (0·3–0·6μ), detected 2–4 hours after infection, were replaced by RNA (rust red) inclusions (1·0–4·0μ) during the next 24 hours. In the course of a further 48 hours these inclusions increased in number, forming clusters; and the staining with acridine orange showed a change from RNA to DNA. DNA-staining particles (mature virus) subsequently became evident. Reinfection occurred, the cycle was repeated and eventually the cell, packed with virus, ruptured, liberating mature virus. The virus colonies were enveloped in an RNA-containing matrix which, obviously, was not part of the virus since it could be removed by ribonuclease, leaving the virus intact. It was, presumably, a metabolic pool provided for the virus by the host cell. Feulgen staining was correlated with the presence of DNA, as was reaction with fluorescein-tagged antibody.

[No mention is made of the *mode* of multiplication of this virus, whether or not by binary fission. In fact the sole advance on previous work is the precise correlation of staining (acridine orange) with the sequence of chemical changes undergone by the developing virus.]

S. P. Bedson

FURNESS, G., GRAHAM, Doris M. & REEVE, P. **The Titration of Trachoma and Inclusion Blennorrhoea Viruses in Cell Cultures.** *J. General Microbiol.* 1960, Dec., v. 23, 613–19.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 523.]

FURNESS, G., GRAHAM, Doris, REEVE, P. & COLLIER, L. H. **The Growth of Trachoma and Inclusion Blennorrhoea Viruses in Cell Culture.** *Rev. Internat. du Trachome.* 1960, v. 37, No. 4, 574–84, 3 figs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 522.]

INOUE, Y., MURAKAMI, K., OHASHI, T. & ARAKAW, S. **The Clinical Value of Complement Fixation Test (CFT) by the Use of Antigen for Trachoma (TR).** *Rev. Internat. du Trachome.* 1960, v. 37, No. 4, 623–34.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 523.]

BROWN, A., ELSNER, Virginia & OFFICER, J. E. **Growth and Passage of Variola Virus in Mouse Brain.** *Proc. Soc. Exper. Biol & Med.* 1960, Aug.–Sept., v. 104, No. 4, 605–8, 1 fig. [10 refs.]

Large doses of variola virus inoculated intracerebrally into mice showed a single peak of multiplication 72 hours after injection. When more than $10^{5.5}$ pock infectious units were inoculated "the virus was uniformly lethal for mice" [no indication is given of when the mice died in relation to the inoculation]. If mice were killed at the peak of the multiplication cycle, virus could be passaged without loss of titre if brain suspension was used; passage of supernatant of centrifuged brain suspensions led to a lower titre which appeared to be stable for at least 5 passages. *Colin Kaplan*

WOODROOFE, Gwendolyn M. & FENNER, F. **Genetic Studies with Mammalian Poxviruses. IV. Hybridization between Several Different Poxviruses.** *Virology.* New York. 1960, Oct., v. 12, No. 2, 272–82, 1 fig. [12 refs.]

Poxviruses inactivated by heat produce hybrids in tissue culture and in mouse brain, only with other poxviruses within a given subgroup. Hybrids occur more readily between closely related viruses. The few markers available make genetic analysis of viruses such as ectromelia, myxoma and fibroma difficult, if not impossible. Virulence is a particularly difficult marker to work with as changes in virulence may be mutations as easily as the result of hybridization. [See also this *Bulletin*, 1958, v. 33, 1091.] *Colin Kaplan*

SHEFFIELD, F. W., BAUER, D. J. & STEPHENSON, Sylvia M. **The Protection of Tissue Cultures by Isatin β-Thiosemicarbazone from the Cytopathic Effects of Certain Pox Viruses.** *Brit. J. Exper. Path.* 1960, Dec., v. 41, No. 6, 638–47, 11 figs. (6 on pl.). [10 refs.]

Experiments with cultures of a strain of embryo rabbit kidney cells (ERK 1) showed quite clearly that isatin β-thiosemicarbazone [this *Bulletin*, 1960, v. 35, 613; 819] protected the cells from the cytopathic effects of neurovaccinia and rabbit pox viruses and, to a less extent, ectromelia virus. The closely related compounds isatin β-semicarbazone and isatin β-amidinohydrazone were without effect, as was the sodium salt of 7-carboxyisatin β-thiosemicarbazone. The protective effect of isatin β-thiosemicarbazone was shown not to be the result of either extra-cellular inactivation of the virus or of interference with adsorption of virus to cells.
Colin Kaplan

WILDY, P., RUSSELL, W. C. & HORNE, R. W. **The Morphology of Herpes Virus.** *Virology.* New York. 1960, Oct., v. 12, No. 2, 204–22, 8 figs. [31 refs.]

The HFEM strain of herpes simplex virus, grown in tissue cultures of HeLa or chick embryo cells, purified and concentrated by ultracentrifugation and by chromatography on calcium phosphate, was studied under the electron microscope, by the phosphotungstate method for negative contrast, [BRENNER and HORNE, *Biochim. et Biophys. Acta.*, 1959, v. 34, 103; this *Bulletin*, 1959, v. 34, (1054)]. Various kinds of particle were observed, many apparently either defective or deformed by manipulation. Complete particles consisted of a core enclosed in a shell or *capsid* made up of numerous subunits or *capsomeres*, and the whole was surrounded by an envelope.

Empty particles filled with phosphotungstate showed the core to be polyhedral and to have an average diameter of 775 Å. The core must be packed by some material which is not nucleic acid since radio-sensitivity measurements on herpes [POWELL, this *Bulletin*, 1960, v. 35, 201] indicated that nuclei acid occupies a smaller volume than that of the core. The capsid was composed of 162 capsomeres, which looked like elongated hollow prisms with polygonal cross-sections, and which were arranged regularly to give 5:3:2 axial symmetry. Evidence is also presented to show that the capsid is icosahedral. It was very stable and was not disrupted by freezing and thawing, *p*H changes, trypsin, ficin, papain, ether, detergents, ultrasonic vibrations or neutralizing antibody. All these treatments reduced virus infectivity and increased the number of empty capsids observed. The envelope appeared to be a membrane varying in shape and size (mean over-all diameter 1800 Å) which often showed projections at intervals round its periphery. It is not known if the envelope is necessary for a virus particle to be infective, and it is possible that it consists of extraneous host material which has collected round the particle on its passage into the cell cytoplasm, [MORGAN *et al.*, *ibid.*, 311].
Janice Taverne

KELLY, R. & GREIFF, D. **The Level of Lactic Dehydrogenase Activity as an Indicator of the Growth of Influenza Virus in the Embryonate Egg.** *J. Exper. Med.* 1961, Jan. 1, v. 113, No. 1, 125–9, 2 figs.

"The relation between time and the levels of lactic dehydrogenase activity of chorioallantoic fluids from embryonate eggs infected with the PR8 strain of influenza virus were determined quantitatively. The mean values, based on 10 determinations for each time interval, followed a sigmoid curve, with the greatest rates of change occurring between 48 and 72 hours after the inoculation of virus. The activities of the fluids from infected eggs at the 72nd hour or later were approximately 18 times higher than those from non-infected eggs. Based on the data above, a qualitative test for the presence of infection with influenza virus was developed."

MIMS, C. A. **An Analysis of the Toxicity for Mice of Influenza Virus. I. Intracerebral Toxicity.** *Brit. J. Exper. Path.* 1960, Dec., v. 41, No. 6, 586–92, 8 figs. on 2 pls. [21 refs.] **II. Intravenous Toxicity.** *Ibid.*, 593–8, 9 figs. on 2 pls.

Adult and some suckling mice were inoculated intracerebrally or intravenously with large doses of MEL or PR8 strains of influenza A virus. "Toxic" deaths

occurred as described by other authors [this *Bulletin*, 1947, v. 22, 213]. Organs were sectioned for routine histological examination and staining for the presence of specific virus antigen by the fluorescent antibody method of Coons. Fluorescence was seen shortly after infection; this faded and then reappeared some hours later. In this way virus infection was detected in the ependymal and meningeal cells of animals inoculated intracerebrally; this did not extend to further cells in adult mice inoculated with standard strains of virus, but when suckling mice were inoculated fluorescence extended into the deeper layers of the ependyma and when a neurotropic strain (NWS) was given to adult mice parenchymal cells became infected.

Attention was concentrated on the livers of intravenously injected mice. At the time of death these were enlarged, red, mottled and friable. Much fluorescent-staining antigen seemed to be taken up by the littoral cells and then disappeared. Subsequently fluorescent staining appeared round the rim of the cytoplasm of hepatic parenchymal cells. These hepatic cells were also successfully infected by inoculation by the biliary tract. It was shown that there was a small increase in the amount of infectious virus in the liver between 8 and 18 hours after intravenous inoculation. Widespread fluorescence was found in suckling mice inoculated intraperitoneally with standard or neurotropic strains.

D. A. J. Tyrrell

Schmidt, B., Hartmann, D. & Grossgebauer, K. Die Gewinnung unterschiedlicher Hämagglutininfraktionen aus Influenzaviren mit Hilfe von DEAE-Zellulose-Ionenaustauscher. [**The Isolation of Different Haemagglutinin Fractions from Influenza Virus with DEAE-Cellulose Ion Exchanger**] *Arch. f.d. gesamte Virusforschung.* 1960, v. 10, No. 3, 361–7, 2 figs. [19 refs.]

Haemagglutinin was prepared from the A2/Sing/1/57 strain of influenza virus by extraction of the infected allantoic fluid with ether, and was then fractionated on a column of N:N′-diethylaminoethylcellulose. Elution was carried out with water, *p*H 7·0 phosphate buffer containing increasing concentrations of sodium chloride, and subsequently with increasing concentrations of sodium hydroxide. The fractions were examined for the presence of haemagglutinin. 3 haemagglutinating fractions were obtained. The first 2 gave higher titres with guineapig than with chick cells, which is known to be characteristic of haemagglutinin dissociated from the virus particles by ether treatment, whereas the third fraction showed no difference in titres, and was considered to be residual haemagglutinin associated with virus. In similar preparations made without ether treatment 2 fractions were obtained which showed no titre difference. *D. J. Bauer*

Wong, S. C. & Kilbourne, E. D. **Changing Viral Susceptibility of a Human Cell Line in Continuous Cultivation. I. Production of Infective Virus in a Variant of the Chang Conjunctival Cell following Infection with Swine or N-WS Influenza Viruses.** *J. Exper. Med.* 1961, Jan. 1, v. 113, No. 1, 95–110, 1 text fig. & 2 figs. on 2 pls. [40 refs.]

Colobert, L. & Fontanges, R., with the technical collaboration of N. Kratchko. Interférence d'un inhibiteur au cours du développement de *Myxovirus parainfluenzae* I (virus Sendaï) en oeuf de poule embryonné. [**Inhibitor Interference in the Course of *Myxovirus parainfluenzae* I (Sendai Virus) development in Embryonated Chicken Egg**] *Ann. Inst. Pasteur.* 1960, Dec., v. 99, No. 6, 839–51, 6 figs. [14 refs.]

An inhibitor of the haemagglutinin and haemolysin of Sendai virus was detected in the allantoic and amniotic fluid of eggs incubated for a total of 11 days or more. The inhibitor is heat stable but destroyed by periodate and RDE. The authors believe it may cause the relatively poor yields of haemagglutinin which were obtained when they attempted to propagate Sendai virus by inoculating eggs incubated for 10 or more days prior to inoculation rather than in eggs incubated for 9 days and harvested 2 days later. *D. A. J. Tyrrell*

Hermodsson, S. **Effect of Ultrasonic Vibration on the Haemaggulinating Activity of some Para-Influenza Viruses.** [Correspondence.] *Nature.* 1960, Dec. 31, v. 188, 1214.

Klemperer, H. G. **Hemolysis and the Release of Potassium from Cells by Newcastle Disease Virus (NDV).** *Virology.* New York. 1960, Dec., v. 12, No. 4, 540–52, 4 figs. [23 refs.]

Schoenfeld, A. & Rannon, L. [**Prevalence of Enteroviruses in Hospitalized Infants and Children during the Summer of 1959**] *Harefuah.* Jerusalem. 1961, Jan. 1, v. 60, No. 1 [in Hebrew 1–3. English summary 3].

The English summary appended to the paper is as follows:—

"From the stools of 292 infants and children hospitalized during the summer of 1959 in the Pediatric Department of Zahalon Hospital, 65 cases (22·2%) gave positive monkey kidney cell cultures of enteroviruses. The percent of isolations was 20·3% in infants up to the age of 6 months, 43·4% from 6 months to 1 year, 34·4% from 1–2 years and only 6·9% in those over the age of 4.

"55·2% of the isolated strains belonging to the ECHO group of viruses, and together with the unidentified strains, probably also of the ECHO virus group, constituted about 70% of all isolations. 10·8% of the enterovirus strains were identified as poliovirus, all type 3.

"Of the 292 children, 140 had gastroenteritis (a), 84 had respiratory diseases (b), 27 had combined gastrointestinal and respiratory symptoms (c), and 41 had other diseases (d). Correlation of the clinical picture with the rate of enterovirus isolation, revealed the following: clinical groups (a) and (b) each showed about 15% of enteroviruses, similar to the rate of isolations in the control group (d). The outstanding finding was the unusually high recovery of enteroviruses, over 80%, from group (c), the cases with combined gastrointestinal and respiratory disease. These findings are preliminary and the problem is being further investigated."

HOLLAND, J. J.; HOYER, B. H.; MCLAREN, L. C.; SYVERTON, J. T. **Enteroviral Ribonucleic Acid. I. Recovery from Virus and Assimilation by Cells** [HOLLAND, HOYER, MCLAREN & SYVERTON]. *J. Exper. Med.* 1960, Nov. 1, v. 112, No. 5, 821–39, 5 figs. [27 refs.] **II. Biological, Physical, and Chemical Studies** [HOLLAND, MCLAREN, HOYER & SYVERTON]. *Ibid.*, 841–64, 9 figs. [29 refs.]

These 2 papers describe experiments with infectious ribonucleic acid obtained by phenol extraction of enteroviruses. Type 1 poliomyelitis virus and Coxsackie B1 viruses were used and HeLa cells were the host system for most of the experiments.

I. The first paper describes a new method of assaying infectious RNA. This achieves approximately 0·1% of the infectivity of the intact virus from which the RNA was derived. This is no better than that described by some other workers [see SPRUNT *et al.*, this *Bulletin*, 1960, v. 35, 204] but was found to be optimal for the authors' cells. First the cells were farmed in human sera containing medium but in setting up assay cultures 20% calf serum was used. RNA was diluted 1/10 in 2·2 M magnesium sulphate and additionally in 2·0 M $MgSO_4$. The RNA was exposed to cultures in 2·0 M $MgSO_4$ in a volume of 0·2 ml. (for 2×10^6 cells) for 12–15 minutes at room temperature. Cultures were then washed and overlaid with agar-containing medium with 20% calf serum. The experimental basis for this choice of method is fully documented. The evidence suggests that high salt concentration acts partly by increasing cell receptivity of RNA and partly by stabilizing the infectious component of the RNA.

II. In the second paper some biological, physical and chemical properties of infectious RNA are compared with those of intact virus. Whereas intact poliomyelitis virus is not adsorbed to dimethylaminoethyl cellulose [DEAE] columns [this *Bulletin*, 1959, v. 34, 954] the infectious RNA is firmly bound and only partially eluted by strong salt solutions. With methionine labelled with ^{35}S it was found that the infectious RNA had lost 90% of the protein during phenol extraction. Infectious RNA was more heat stable than intact virus and was not inactivated by agents disrupting hydrogen bonds (8 M urea or 6 M guanidine) or disulphide bonds (0·3 M thioglycolate or 1 M mercaptoethanol). Chloroform alone also had no effect but when supplemented with octanol infectivity of RNA was reduced, but without altering the sedimentation characteristics of the RNA. Both ribonuclease and snake venom phosphodiesterase gave first order inactivation curves for infectious RNA. Bacterial alkaline phosphate was without effect on RNA infectivity nor did it influence subsequent phosphodiesterase activity. Hydroxylamine (0·1 M) rapidly destroyed infectivity in viral RNA without depolymerizing the RNA. Other carbonyl reagents, semicarbazide, hydrazine, azide and cyanide, were without significant effect on RNA infectivity. It is concluded that RNA infectivity is a property of a single intact strand of RNA and attempts to demonstrate effective sub-units of this RNA were unsuccessful. Infectious RNA was found to develop just prior to, but in parallel with, fully intact virus as demonstrated in HeLa cells infected under conditions of a single growth cycle experiment with poliomyelitis virus. *A. J. Beale*

POLSON, A., HAMPTON, J. W. F. & DEEKS, D. **Zone Electrophoresis of Poliovirus partially inactivated by Formaldehyde.** *J. Hygiene.* 1960, Dec., v. 58, No. 4, 419–25, 4 figs. & 2 pls.

Zone electrophoresis of living type 2 (MEF1) poliomyelitis virus and a concentrate of virus partially inactivated with formaldehyde was carried out in 35% cane sugar in borate buffer, *p*H 8·6. It was found that the mobility of partially inactivated virus was greater than for living virus. This applied to all the virus, no separation of formaldehyde-killed and residual living virus was effected by the zone electrophoresis. The zone containing maximum infectivity of partially inactivated virus also contained the maximum amount of virus antigen detectable by production of neutralizing antibodies or precipitin tests in agar gel. *A. J. Beale*

DUBES, G. R., CHAPIN, Margaret & TOLBERT, O. **The Genetic Relationship between Thermostability of Poliovirus and its *in vivo* Response to Cystine.** *Arch. f.d. gesamte Virusforschung.* 1960, v. 10, No. 3, 315–34, 6 figs. [10 refs.]

This paper reports a detailed analysis of mutants and back mutants of a strain of type 1 poliomyelitis virus, Akron ($+^{cr}$), which requires cystine for growth but is not inhibited by it and is also thermostable. The 3 mutant strains are: cr, which neither requires nor is inhibited by cystine; cr^{si}, which does not require cystine but is slightly inhibited by larger doses; and cr^{i}, which does not require cystine and is markedly inhibited by it. Cystine inhibition is made manifest by plaque appearance. Inhibited strains show clear plaques without cystine but turbid plaques (due to surviving cells in the plaque) in the presence of cystine. A wild type Brunhilde strain heat-stabilized by cystine in the medium and a thermostable mutant t^r derived from it was also studied [see POHJANPELTO, this *Bulletin*, 1959, v. 34, 294]. It was found that cystine inhibition and thermostability were closely correlated characters being almost certainly twin manifestations of one genetic element. Cystine requirement in general is negatively correlated with cystine inhibition and thermostability but exceptions occur. Cystine-requiring strains are thus, in general, thermolabile, but this thermolability in the absence of cystine does not explain their requirement for cystine. There may be a cystine-stabilized heat labile virus precursor, however, but since some cystine-requiring strains are nonetheless heat stable (without added cystine) this seems an unlikely solution. Cystine inhibition (*i.e.* sparing of cells) occurs at some post-adsorption step in virus multiplication. It is not a direct action on either cell or virus. It is suggested that cystine may act as an antimetabolite for an essential viral precursor. *A. J. Beale*

KOCH, G. **Influence of Assay Conditions on Infectivity of Heated Poliovirus.** *Virology.* New York. 1960, Dec., v. 12, No. 4, 601–3, 1 fig.

PACCAUD, M. F., PONGRATZ, E. & SCHLAEPFER, J. La microréaction de floculation sur lame par la technique de double diffusion en agar entre anticorps et antigènes poliomyélitiques. I. Étude de la réaction. **[Microtechnique for Slide Precipitation Tests in Agar with Poliomyelitis Antigens and Specific Antisera. I. Study of the Reaction]** *Arch. f.d. gesamte Virusforschung.* 1960, v. 10, No. 3, 335–50, 6 figs. [24 refs.] II. Étude comparative des anticorps neutralisants, fixant le complément et floculants. **[II. Comparative Study with Neutralizing, Complement-fixing and Precipitating Antibodies]** *Ibid.*, 351–60. [10 refs.]

I. A microtechnique for performing precipitin tests in agar with poliomyeltitis virus preparations and specific antisera is described. This involves the use of agar on a glass microscope slide and a pattern of holes is cut with a special tool [see GRASSET *et al.*, this *Bulletin*, 1958, v. 33, 534]. The reactants are added to the cups and left at room temperature in a humidified box for 16–24 hours and then the precipitin lines are stained. With this technique, 2 specific precipitin lines can be detected in many poliomyelitis virus preparations, as previously described by LE BOUVIER [*ibid.*, 1960, v. 35, 316]. [The 2 lines correspond to those called C and D, being here called inferior and superior lines, respectively.] No group-specific lines were detected. The antigen for use in these tests had to be concentrated at least 50-fold. Treatment of virus preparations with formalin removed the inferior flocculation line. In human sera both these 2 precipitin lines sometimes occur but, in general, the inferior line (C) appears early after infection and declines early whereas the superior (D) line appears later and persists longer.

II. Investigation of sera of individuals after recent poliomyelitis virus infection or inoculation with killed vaccine was performed by the neutralization, complement-fixation and precipitin tests. In general, there was little correlation between the presence of antibodies by the complement-fixation and precipitin techniques. There was much more correlation between neutralization and precipitin tests. Thus, after natural infection, most individuals had antibodies detectable by both methods, but in vaccinated subjects there was less correlation. For example, before vaccination for type 1, 13·7% had neutralizing but not flocculating antibodies and 17·1% had the reverse pattern; after vaccination the figures were 23·6% and 1·7%. These discrepancies occur both with the superior and inferior lines. It is concluded that antibodies detected by the precipitin test differ from those detected by complement fixation or neutralization.

A. J. Beale

GREEN, R. H. & OPTON, E. M. **A Micromethod for Determination of Poliovirus Antibody suitable for Mass Surveys.** *Amer. J. Hyg.* 1960, Sept., v. 72, No. 2, 195–203, 6 figs. [12 refs.]

An ingenious method of performing poliomyelitis virus antibody titrations on blood samples collected by heel or finger prick is described. Blood is adsorbed onto sterilized filter paper marked out into 16 squares, each of 1 cm. The filter paper is thoroughly soaked with blood and this requires obtaining a fairly free flow from the prick and needs a certain amount of patience. The specimens are returned to the laboratory in sterilized envelopes and then stored at 4°C. in a desiccator. In the laboratory the squares are cut out and 3 are used for each type of virus. One square is placed into a tube and graded doses of virus are added, 50, 500 and 5,000 tissue culture doses in 0·3 ml. of Hanks solution. Thereafter an additional 0·3 ml. of Hanks solution is added and the filter paper macerated with the tip of a pipette and shaken for 1¼ hours at room temperature. 0·1 ml. quantities of the mixtures from each tube are taken into each of the 3 monolayer cultures of monkey kidney cells and observed for cytopathic effects after incubation at 37°C. The end-points are read at 4 days.

In preliminary tests it was found that there was a good correlation between antibody titre assayed in the conventional fashion and absence of antibody as judged by failure to inhibit 50 tissue culture doses and the presence of increasing amounts of antibody up to a high level indicated by inhibition of 5,000 tissue culture doses of virus. In general, those with a low level of antibody shown by inhibition only of 50 tissue culture doses, had serum titres of 1 in 16 or less. Sera that inhibited 500 tissue culture doses were found to have a titre in the range of 1 in 32 to 1 in 128 and those with a high level had titres of 1 in 256 or greater. Therefore, on this basis, a more or less arbitrary estimate of the titre was arrived at according to the pattern of response of the 3 tubes mixed with each of the 3 dilutions of virus. Thus, if 1 tube only was protected with 50 tissue culture doses then the titre was 1 in 4, if 2 tubes were protected 1 in 8, if all 3 tubes were protected 1 in 16, if in addition 1 tube was protected with 500 tissue culture doses then the titre was 1 in 32 and so on in progression up to a titre of 1 in 1,024 or greater. It was found that in general the procedure gave a reasonably accurate assay of the amount of poliomyelitis virus antibody in a preparation. Most of the work was done with type 1 poliomyelitis virus but it is stated that similar results can be obtained with type 2 and type 3. Other methods of titrating the serum present in the blood soaked on the filter paper squares have also been tried but as yet none appears as promising as the method described. The great advantage of this method apart from its simplicity is that it has proved readily acceptable to parents in field trials which is far from being the case with venipunctures.

[See also this *Bulletin*, 1958, v. 33, 412; 1959, v. 34, 690.] *A. J. Beale*

BEURLIN, G., MEYER, J. & MALGRAS, J. Mise en évidence des précipitines dans les immunsérums poliomyélitiques. **[Demonstration of Precipitins in Poliomyelitis Immune Sera]** *Rev. d'Immunologie.* 1960, July–Sept., v. 24, No. 4, 512–20, 3 figs.

Rabbits were immunized with a 5-fold concentrate of type 1 (Mahoney) poliomyelitis virus inactivated with formalin. 2 rabbits received vitamin B5 also and 2 did

not. In addition, 2 rabbits were immunized with killed poliomyelitis vaccine made by the Institut Pasteur. Sera obtained during the immunization course were tested for CF and precipitating antibodies against type 1 virus. The micromethod of GRASSET *et al.* [this *Bulletin*, 1958, v. 33, 534] was used for precipitin tests. Precipitating antibodies were found in later bleedings than CF antibodies and the precipitin lines were most pronounced in animals receiving vitamin B5. As many as 4 precipitin lines were seen and the analysis of these is being undertaken. The precipitin lines were less strong in rabbits given the Institut Pasteur killed poliomyelitis vaccine. *A. J. Beale*

HALONEN, P. & HUEBNER, R. J. **ECHO and Poliomyelitis Virus Antisera prepared in Guinea Pigs with Fluorocarbon-Treated Cell Culture Antigens.** *Proc. Soc. Exper. Biol. & Med.* 1960, Oct., v. 105, No. 1, 46–9.

The preparation of specific viral complement fixing antisera in laboratory animals is often marred by cross reactions due to the sera containing antibodies to the host cell. This problem can be overcome by pretreatment of the viral antigen with fluorocarbon [see, for example, HALONEN *et al.*, this *Bulletin*, 1958, v. 33, 893]. In this paper it is reported that fluorocarbon-treated antigen produces specific antisera in guineapigs with many enteroviruses. Treated tissue culture virus gives a specific viral CF titre 16-fold higher than the host cell antigen. If untreated viral antigen is used the viral antigen gives only an approximately 2-fold higher titre than the host cell antigen. It was found that fluorocarbon was not universally successful in removing host cell antigen and pretesting of the antigens against host cell immune serum before inoculation is recommended. The fluorocarbon-treated antigen must also be tested for specific activity since it appears that such treatment destroys the antigenicity of at least ECHO types 15–19. *A. J. Beale*

IONESCU-MIHĂIEŞTI, C., CIUCĂ, A., MESROBEANU, I., WISNER, B., HORODNICEANU, F., SERGIESCO, Dina, KLEIN, R., ZAMFIRESCO, M., GANCEVICI, G., ARION, R., STOIAN, I., FÉNYVES, A. & GAICO, N. **Some Data concerning the Preparation of Inactivated Poliovaccine on an Experimental Scale.** *Arch. Roumaines Path. Expér. et Microbiol.* 1960, Sept., v. 19, No. 3, 321–8, 1 fig. [17 refs.]

Experience in Rumania in the production of killed poliomyelitis vaccine is described. The satisfactory manufacturing experiences of safe and immunologically potent vaccine has led to large scale production of the vaccine in Rumania in 1960. Superior virus titres were obtained in trypsinized cell cultures compared with cultures of the Maitland type. Since the latter method also produces more monkey kidney antigen and is more expensive it should be dropped in favour of the former method. The Mahoney strain of type 1 was found to be "considerably" superior to the Brunenders strain in antigenic potency and was therefore employed. The safety of properly prepared vaccine containing the Mahoney virus is now thoroughly established. In order to prepare safe killed poliomyelitis vaccine, measures to remove clumps of cellular débris or virus aggregates are required or methods of inactivation that can penetrate to virus embedded in such aggregates must be devised. The authors note that the commonly used Seitz pads adsorb virus but confirm that pretreatment with gelatin prevents this. They also confirm the late appearance of cytopathic effects with poliomyelitis virus treated with formalin. In blending the final vaccine, account is taken of the greater importance of type 1 poliomyelitis virus in the aetiology of paralysis and the relatively poorer potency of this component. Monovalent vaccine is therefore blended into final vaccine in the following proportions by volume: type 1, 3 parts; type 2, 1 part; type 3, 2 parts. Using an antigen extinction type of antigenic potency titration in guineapigs, based on the method of GARD [this *Bulletin*, 1959, v. 34, 586] the authors found that Rumanian vaccine was superior in potency to several batches of foreign vaccine including 1 adsorbed with aluminium phosphate. *A. J. Beale*

ROCA-GARCIA, M., ORSI, E. V., JERVIS, G. A., MARKHAM, F. S., BACIGALUPI, J. C., DOANY, Hanna, TOSI, H., CABASSO, V. J., MOYER, A. W. & COX, H. R. **Laboratory Studies associated with Field Trials of Monovalent Oral Poliovirus Vaccines.** *J. Infect. Dis.* 1960, Nov.–Dec., v. 107, No. 3, 300–317, 16 figs. [16 refs.]

The material in this paper was presented on June 26 1959, at the First International Conference on Live Poliovirus Vaccines sponsored by the Pan American Health Organization and the World Health Organization —see this *Bulletin*, 1961, v. 36, 276.

WENNER, H. A., KAMITSUKA, P. S., SOERGEL, Marjorie & LENAHAN, Margaret. **Antigenic Variations among Type 1 Polioviruses. Resistance of Vaccinated Monkeys to Wild-Type Poliovirus.** *Amer. J. Hyg.* 1960, Nov., v. 72, No. 3, 261–74, 3 figs. [12 refs.]

The authors have previously described antigenic differences among type 1 poliomyelitis viruses [this *Bulletin*, 1959, v. 34, 1301] and wondered whether the more marked differences may be sufficient to circumvent the protective effect of killed poliomyelitis vaccine. Monkeys were therefore immunized with small graded doses of a type 1 (Mahoney) inactivated vaccine. The animals were divided into 2 groups paired on the basis of similar antibody titre (gauged by inhibition of cytopathic effect) and challenged by intramuscular inoculation with approximately 100 PD50 (paralytic doses) of Mahoney or Wiersma strains of type 1. Wiersma showed quite marked antigenic differences from Mahoney. The results of challenge failed to reveal any relative lack of protective effect against Wiersma compared with Mahoney induced by the Mahoney vaccine. Monkeys with antibodies detectable by inhibition of cytopathic effects were solidly

immune to paralysis although 3 out of 26 developed central nervous lesions following challenge with Mahoney virus. Many animals without antibodies detectable in this way were also protected but most of these animals probably had low titres of antibodies since such antibodies could be detected in some by the sensitive plaque reduction technique. After one 1 ml. dose of vaccine the antibody response of individual monkeys was very variable both in titre and time required to develop detectable and maximal levels of antibodies. These discrepancies were much less if one 5 ml. dose was employed. *A. J. Beale*

ROBBA, L. & VIRAT, J. Préparation d'antigènes pour la déviation du complément dans le diagnostic sérologique des affections à virus Coxsackie, groupe B. **[Preparation of Antigens for Serological Diagnosis of Coxsackie B Infections by means of Complement Fixation]** *Ann. Inst. Pasteur.* 1960, Nov., v. 99, No. 5, 784–94. [32 refs.]

After a useful review of the methods of preparing Coxsackie complement-fixing antigens, a method for preparing satisfactory CF antigens of Coxsackie B viruses is described. The virus is grown in KB cells in 2·5% calf serum. The best antigen was made by freezing and thawing the cells 8 times, when the cytopathic effect was complete, in 1/50 volume of media and then clarifying by low-speed centrifugation. The antigen was then treated with an equal volume of ether for 5 minutes and the aqueous phase used as antigen. With Coxsackie B1-5, satisfactory antigens were made and tested against rabbit antisera to all except Coxsackie B2. In addition to specific fixation some cross-reactions occurred, suggesting shared antigens between Coxsackie B types. Some sera fixed complement with the normal cell antigen, but treatment of antigens with ether overcame this effect.

[The experiments are described in detail but their planning was not very comprehensive.] *A. J. Beale*

BURNSTEIN, T. **Relative Susceptibility of Young Mice and Hamsters to Coxsackie B-3 Virus.** *Proc. Soc. Exper. Biol. & Med.* 1960, Nov., v. 105, No. 2, 306–8, 1 fig.

"Hamsters were more susceptible than mice to a strain of Coxsackie B-3 virus. This was shown by comparing the response of these species to virus as influenced by age. At a given age a stock virus preparation showed a consistently higher titre in the hamster. Furthermore, the period of susceptibility of hamsters was about twice that of mice."

YOHN, D. S. & HAMMON, W. McD. **ECHO-4 Viruses: Improved Methods and Strain Selection for Identification and Serodiagnosis.** *Proc. Soc. Exper. Biol. & Med.* 1960, Oct., v. 105, No. 1, 55–60. [14 refs.]

Neutralization tests are unreliable with ECHO 4 virus when the result is assessed by observing cytopathic effects in tube cultures. This applies both to antibody titrations on patients' sera and also in tests to identify unknown virus with specific ECHO 4 antisera prepared in animals. The first problem has been overcome by the discovery of strains of ECHO 4 virus that are satisfactorily neutralized in tube titrations. The authors confirm that the DuToit strain of BARRON and KARZON (*Federation Proc.* Wash., 1960, v. 19, 406) is one such strain and describe a new strain, 5705, which is also satisfactory for this purpose. Plaque-forming strains of ECHO 4 can also be used with the plaque-reduction technique [this *Bulletin*, 1958, v. 33, 532] of antibody titration. This technique will also serve to identify plaque-forming strains. The main bulk of ECHO 4 viruses are most satisfactorily identified by using a CF test. Here more difficulties occur. First, antigens prepared in monkey kidney cells are often anticomplementary; this problem was found to be minimized by the use of Eagle's basal medium for virus growth. Second, antisera to virus grown on monkey cells contain anticellular antibodies (they may also contain antibodies to simian virus, *e.g.* vacuolating virus [SWEET and HILLEMAN, *Proc. Soc. Exper. Biol. & Med.*, 1960, v. 105, 420; this *Bulletin*, 1961, v. 36, May] which give rise to fixation of complement not due to ECHO 4. It was found that ECHO 4 viruses could be adapted readily to Detroit 504 cells [as first described by STULBERG *et al.*, *ibid.*, 1958, v. 33, 716]. Immunizing antigens prepared from viruses grown on these cells gave antisera in guineapigs and monkeys which did not react in CF tests with normal monkey kidney cell tissue culture antigen. Such sera were satisfactory for identifying ECHO 4 viruses freshly isolated in monkey kidney cells.

[The problem can be partially solved by using virus treated with fluorocarbon as immunizing antigen which minimizes host cell antibody production, see HALONEN and HUEBNER, p. 410, and HAMMON *et al.*, *ibid.*, 1959, v. 34, 837]. *A. J. Beale*

GOVAERTS, A. **Infectious Canine Hepatitis and Human Hepatitis.** *Arch. f.d. gesamte Virusforschung.* 1960, v. 10, No. 3, 395–8. [18 refs.]

Canine hepatitis virus could be maintained in primary explant cultures of dog kidney cells and attained titres of 5·3 log units per ml. Some multiplication was also obtained in cultures of HeLa and T (human kidney) cells. In neutralization tests carried out on 10 sera with 30 TCD50 of virus, antibody in titres of 10–80 was found in the sera of 1 of 3 patients suffering from infective hepatitis and of 2 persons having frequent contact with dogs.

D. J. Bauer

MORGAN, C., HOWE, C. & ROSE, H. M. **Structure and Development of Viruses as observed in the Electron Microscope. V. Western Equine Encephalomyelitis Virus.** *J. Exper. Med.* 1961, Jan. 1, v. 113, No. 1, 219–34, 28 figs. on 15 pls. [43 refs.]

SHUBLADZE, A. K. & BYCHKOVA, E. N. **An Experimental Study of a Tissue Culture Vaccine for the Prophylaxis of Tick-Borne Encephalitis.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1960, v. 31, No. 2, 203–9. [Translated from Russian.]

The IAS and UKH 10 strains of Russian spring-summer encephalitis virus were grown in chick embryo fibroblast cultures. They were infected with seed virus titring at least 10^6 derived from mouse brain or chick embryos. The highest titres (10^5–10^7) in the culture fluids were found after 4–6 days. Maximum titre was reached a day earlier when the cultures were infected immediately they were set up. The virus was most successfully inactivated by using 1:200 formalin at *p*H 7·0 and 18–20°C. for 5 days. No virus was detected after 12 hours by inoculation of 0·03 ml. intracerebrally into mice. 11 batches of vaccine were prepared with a total volume of 16 litres. After inactivation 0·03 ml. intracerebrally and 0·25 ml. intraperitoneally were inoculated into 30 mice and 3 blind passages made. No live virus was detected. Mice were immunized intraperitoneally with 3 doses of 0·5 ml. at 2-day intervals [the translation is not clear: "3 times every second day"] and challenged intraperitoneally 12 days later. 9 batches of vaccine gave resistance indices ranging from 131 to 128,000. Sera from immunized mice and rats were also examined and found to contain neutralizing antibody. 24 volunteers were given 2 doses of 1–3 ml. of potent vaccine with a 20-day interval and a similar dose after 40 days. 3 volunteers had neutralizing antibody before vaccination: all except 7 had significant levels after 2 doses and 2 more probably had antibody: 2 of the remainder were tested after 3 doses and had neutralizing antibody in high titre. More marked local erythema and swelling were seen after intradermal than after intramuscular inoculation. 7 volunteers had febrile reactions. The vaccine was stored at 4°C. for 4 months without loss of potency.

C. E. Gordon Smith

VARMA, M. G. R., WEBB, H. E. & PAVRI, K. M. **Studies on the Transmission of Kyasanur Forest Disease Virus by *Haemaphysalis spinigera* Newman.** *Trans. Roy. Soc. Trop. Med. & Hyg.* 1960, Nov., v. 54, No. 6, 509–16.

Kyasanur Forest disease (KFD) virus has been isolated 14 times from *Haemaphysalis spinigera* and once each from *H. turturis* and *H. papuana* [this *Bulletin*, 1959, v. 34, 870]. *H. spinigera* has been shown to infest birds, monkeys and rodents which are susceptible to the virus and also cattle and buffaloes with antibody to it. In these experiments the G11338 strain of KFD virus was used after 3 mouse-brain passages and 6 blood-passages in chicks 1–4 days old. Larval *H. spinigera*, the progeny of adults collected as nymphs from an uninfected area, were infected by feeding on chicks circulating virus. Ticks were allowed to feed from 1½ days after the chicks had been infected. The chicks circulated about 3 log mouse ICLD50 2 days after inoculation, 4·3–5·0 log on the 3rd day, 3·3–4·5 on the 4th, 4·0 on the 5th and 2·7 on the 6th day after infection. After feeding, the ticks were maintained at 80–90% humidity and 21·0–35·5°C. Larvae were shown to be infected immediately after feeding and in the moulting phase. In 4 batches of unfed nymphs, 20–56 days after infection as larvae, 5/6, 3/5, 3/4 and 4/8 pools yielded virus. 30–40 days after infection virus titres in the nymphs varied from $<5{\cdot}0$ to 6·8 log. After moulting to adults, males and females were tested for virus and both found infected—overall infection rates varied from 25–70% and the virus titres in the ticks from $<3{\cdot}6$–6·0 log 78–160 days after infection. Unfed nymphs infected as larvae transmitted to chicks 24–73 days after infection. From 13 of 25 chicks with evidence of transmission all the nymphs released were recovered, thus infection by ingestion of ticks or by scratching can be disregarded. Adult ticks 126–127 days after infection were fed on a buffalo and transmitted. A second tick-chick cycle of transmission by feeding was successful.

[In the title of the paper, "*Haemaphysalis spinigera* Newman" should read "*Haemaphysalis spinigera* Neumann".] *C. E. Gordon Smith*

TURNER, W., BIGLEY, Nancy J., DODD, M. C. & ANDERSON, G. **Hemagglutinating Virus isolated from Cat Scratch Disease.** *J. Bacteriology.* 1960, Oct., v. 80, No. 4, 430–35, 1 fig.

Allantoic fluid from eggs which had earlier been inoculated with pus from infected lymph nodes from cases of cat-scratch disease agglutinated red cells from rabbits and from hooded rats. Zoning phenomena suggested that an inhibitor was present in allantoic fluid, and both haemagglutinin and inhibitor appeared to be sensitive to ionic concentration. The inhibitor was removed by diluting allantoic fluids into 0·28M glucose and centrifuging.

Normal rabbit and human serum also contained an inhibitor. This was eliminated by extracting with acetone and reconstituting the serum proteins in a mixture of phosphate buffer and HCl. Reconstituted sera from immunized rabbits and from 2 out of 3 human cases of cat-scratch fever specifically inhibited haemagglutination. Rabbits did not produce specific antibody after immunization with haemagglutinating fluids unless the fluids had been treated with glucose to remove the inhibitor.

Herpes simplex antiserum was found to inhibit the haemagglutination. However, the haemagglutinating virus did not kill chick embryos even after passage, "had no cytopathogenicity for cells in tissue culture" [no details given] and did not cause lesions on the rabbit cornea. *Janice Taverne*

HANNOUN, C. & PANTHIER, R. Application de la méthode des plages en cultures cellulaires à l'étude du virus-vaccin amaril 17D. [**Application of the Plaque Technique to the Study of 17D Yellow Fever Virus**] *Bull. Soc. Path. Exot.* 1960, May–June, v. 53, No. 3, 424–30, 7 figs. on 2 pls.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1961, v. 58, 437.]

De Groot, Carmen J., Metzger, J. F., Smith, C. W. & Hoggan, M. D. **Demonstration of Yellow Fever Virus in Human Cell Culture by Immunofluorescence.** *Virology.* New York. 1960, Oct., v. 12, No. 2, 317–20, 2 figs.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1961, v. 58, 308.]

Ado, A. D. & Kanchurin, A. K. **Problem of the Allergenic Properties of Fermi Rabies Vaccine.** *Problems of Virology.* London. 1960, v. 5, No. 1, 13–19. [15 refs.] [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin,* 1961, v. 58, 311.]

IMMUNITY

La Via, M. F., Uriu, S. A., Barber, Nancy D. & Warren, Anne E. **Effect of β-3-Thienylalanine on Antibody Synthesis. I. Preliminary *in vitro* and *in vivo* Studies.** *Proc. Soc. Exper. Biol. & Med.* 1960, Aug.–Sept., v. 104, No. 4, 562–5, 1 fig. [19 refs.]

β-3-thienylalanine [β-3-TA], when fed to rats in the absence of dietary phenylalanine, results in an almost complete inhibition of antibody response to a single intravenous injection of an antigen (Wissler *et al.*, *Arch. Pathology,* 1956, v. 62, 62). The objects of this paper were to study the effects of β-3-TA on antibody synthesis in tissue culture and to ascertain at what stage in the process of antibody synthesis its inhibitory effect is manifested.

Addition of β-3-TA to a tissue culture system in which spleen fragments were synthesizing antibody did not alter the final antibody output. Spleens for tissue culture were explanted 3 days after injection of antigen, and marked inhibition of antibody formation under normal tissue culture conditions followed the feeding of β-3-TA to donor rats during the induction period.

The restriction of the inhibitory activity of β-3-TA to the early stages of antibody synthesis was confirmed by *in vivo* experiments. *John R. Norris*

Kienitz, M., Ritzerfeld, W. & Sebers, R. Tierexperimentelle Studien zum Problem der natürlichen Resistenz gegenüber bakteriellen Infektionen. I. Mitteilung. Die Erzeugung einer Staphylokokken Sepsis bei der weissen Ratte nach Verabreichung von Fremdeiweiss. [**Animal Experiments on the Problem of Natural Resistance to Bacterial Infection. I. Production of Staphylococcal Septicaemia in the White Rat after Administration of Egg Albumin**] *Ztschr. f. Hyg. u. Infektionskr.* 1960, v. 147, No. 1, 15–27, 4 figs. [34 refs.] II. Mitteilung. Die Behandlung der Staphylokokken-Sepsis eiweissvorbehandelter Ratten mit antitoxischem Staphylokokken-Serum und Serum gesunder Ratten. [**II. Treatment with Staphylococcal Antiserum and Normal Rat Serum of Staphylococcal Septicaemia in Rats previously prepared with Egg Albumin**] *Ibid.,* 28–37. [27 refs.]

I. The intravenous injection of 2 doses each of 0·2 ml. of egg white at a 10-day interval altered the response of white rats to the intravenous injection of staphylococci. In untreated rats the injection had no effect; in treated animals 2 injections of 6×10^5 cocci were often followed by the development of signs of septicaemia with paralysis of the hind legs and signs of nervous system involvement, and in many cases by death. It seemed that the egg white had a damaging effect on the kidneys, producing a type of nephrosis.

II. Neither Behring staphylococcal antitoxic serum nor normal rat serum had any effect on the development of disease after the intravenous injection of staphylococci in animals prepared by the injection of 2 doses of egg white. *R. E. O. Williams*

Kienitz, M. & Kümmel, J. Untersuchungen zur diaplazentaren Übertragung von Antihämolysinen. [**Experiments on the Diaplacental Transmission of Antihaemolysins**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1960, Aug., v. 120, No. 2, 106–19. [48 refs.]

The titre of antibody to staphylococcal α-toxin and to streptolysin O was measured in the retroplacental blood of 32 mothers and in the cord blood of their infants. In only 1 pair was α-antitoxin higher in the mother than in the infant, in 24 it was lower; for antistreptolysin the figures were 5 and 23. Neither antibody was found in significant amounts in amniotic fluid. There is extensive discussion of these results, with a suggestion that antibody may be formed in the placenta.

R. E. O. Williams

Goodman, J. W. & Kabat, E. A. **Immunochemical Studies on Cross-Reactions of Antipneumococcal Sera. III. The Effect of Variation in Molecular Weight on the Cross-Reactivity of Dextran with Type II Antipneumococcal Serum.** *J. Immunology.* 1960, Oct., v. 85, No. 4, 342–6, 2 figs. [25 refs.]

Quantitative immunochemical methods were applied to a study of the cross-reactions between horse or rabbit anti-pneumococcal type II serum (anti-S11) and a series of dextran fractions of graded molecular weight (ranging from approximately 10,000 to 400,000). There was a gradual decrease in precipitating power with decline in

molecular weight. The cross-reaction of horse anti-S11 and the dextran fraction (M.Wt.10,000) was inhibited by certain oligosaccharides; the upper limit in inhibiting power was found with isomaltopentaose. [See also this *Bulletin*, 1960, v. 35, 1150.] *H. Gooder*

HAYDEN, Alonza R. & BECKER, E. L. **Antigen-Antibody Reactions in Agar. V. Precipitate Density Studies using the Oudin Technique.** *J. Immunology.* 1960, Dec., v. 85, No. 6, 591–602, 8 figs. [11 refs.]

HINZ, C. F., Jr., WEDGWOOD, R. J., TODD, E. W. & PILLEMER, L. **The Properdin System and Immunity. XIV. The Injection of Human Properdin into Rabbits and the Production of Antibodies to Properdin.** *J. Immunology.* 1960, Dec., v. 85, No. 6, 547–58, 7 figs. [28 refs.]

ENDERS, J. F. **A Consideration of the Mechanisms of Resistance to Viral Infection based on Recent Studies of the Agents of Measles and Poliomyelitis.** *Trans. & Studies of College of Physicians of Philadelphia.* 1960, Oct., v. 28, No. 2, 68–79, 6 figs. [20 refs.]

After enumerating the non-specific mechanisms responsible for resistance to viral infections, the author deals more fully with two: the depressive effect of pre-existing disease and the production of a non-specific viral inhibitory factor (VIF) by tissue cells exposed to virus. The course of measles virus infection is radically altered in children already suffering from chronic disease; 3 children, one with pancreatic fibrosis, one with myeloid leukaemia, and one with Letterer-Siwe's disease, exhibited no signs of measles but died of Hecht's giant cell pneumonia, and in each case at autopsy the measles virus was recovered from various tissues [this *Bulletin*, 1960, v. 35, 681]. 4 other children, all with leukaemia, developed obvious measles following exposure; all 4 also developed interstitial pneumonitis, which in 2 terminated fatally [*ibid.*, 682]. Reflections of a serious defect in the mechanism of resistance were the unusually long survival of the measles virus in the respiratory tract, a negative complement-fixation test, and the presence of only traces of neutralizing antibodies in the blood. The reasons for this defect are obscure; there was no evidence of a concomitant infection, agammaglobulinaemia or other disturbance of protein synthesis.

Summarizing the discovery of interferon by ISAACS and LINDENMANN [this *Bulletin*, 1957, v. 32, 1203], the author surveys the work [*ibid.*, 1960, v. 35, 315] on a "viral inhibitory factor" (VIF) capable of inhibiting the cytopathogenic activity of a chick-adapted Type II poliovirus on human kidney cells, and in many ways similar to interferon. VIF did not interfere with the adsorption of virus to cell; it appeared to diminish the intracellular synthesis of virus; and somehow it retarded the spread of infection through a cell population. Recently it has been shown that human cell cultures inoculated with an attenuated strain of measles virus produce 2–4 times as much VIF as cultures inoculated with a virulent strain: the author wonders if attenuation of virulence could be correlated with an increased capacity to stimulate *in vivo* the production of VIF.

D. A. Cannon

TRAUB, E. **Demonstration, Properties and Significance of Neutralizing Antibodies in Mature Mice Immune to Lymphocytic Choriomeningitis (LCM).** *Arch. f.d. gesamte Virusforschung.* 1960, v. 10, No. 3, 289–302. [18 refs.]

An improved technique has been developed which facilitates the detection of neutralizing antibody to lymphocytic choriomeningitis virus in adult mice immunized to the virus by subcutaneous or contact infection followed by hyperimmunization by 1 or more injections by the intracerebral route. In intracerebral neutralization tests, neutralization could be observed when the virus-serum mixtures were first incubated at 37°C. for 15 hours. Similar results were obtained in intraperitoneal injection, although in both cases extensive thermal inactivation of the virus occurred. Neutralization of up to 250 ID50 of virus could be observed. Very little transferred immunity was found in the litters born to immune females. In view of the low titres obtained in the improved neutralization test it is suggested that the immunity in mice to lymphocytic choriomeningitis depends on some factor other than antibody. *D. J. Bauer*

TRAUB, E. **Observations on Immunological Tolerance and "Immunity" in Mice infected congenitally with the Virus of Lymphocytic Choriomeningitis (LCM).** *Arch. f.d. gesamte Virusforschung.* 1960, v. 10, No. 3, 303–14. [14 refs.]

The author has previously shown [this *Bulletin*, 1939, v. 14, 174] that mice infected with lymphocytic choriomeningitis virus *in utero* produce large amounts of virus throughout life while showing no signs of illness, and in the present work a further study has been made of this phenomenon. In preliminary experiments it was found that the complement-fixation and infectivity titres of organ extracts were roughly parallel, and the complement-fixation test was then used subsequently for quantitative determinations of the amount of virus. By this means it was found that the organs of mice infected *in utero* which were tolerant to the infection contained much greater amounts of complement-fixing antigen than non-tolerant animals infected for the first time at the age of 5 weeks. The highest titres (up to 132) were obtained with extracts of the spleen, lymph nodes, liver and uterus. The virus antigen persisted indefinitely in the tolerant mice, but declined rapidly in non-tolerant mice which survived infection. The serum of the latter contained complement-fixing antibody. Tolerant mice showed a slight resistance to infection with equine encephalomyelitis virus which was ascribed to interference; when immunized to this virus they responded with a normal production of inhibiting antibody. Tolerant mice also showed considerable resistance to infection with another strain of lymphocytic choriomeningitis virus which was distinguishable by a difference in pathogenicity for infant mice. *D. J. Bauer*

BALTCH, Aldona L., OSBORNE, Winifred, BUNN, P. A., CANARILE, L. & HASSIRDJIAN, Ann. **Serum Complement and Bacteriophage Neutralization Titers in Human Infections, Leukemias, and Lymphomas.** *J. Lab. & Clin. Med.* 1960, Oct., v. 56, No. 4, 594–606, 4 figs. [37 refs.]

The degree of neutralization of phage T2 by normal serum has been considered to be a measure of the amount of properdin in the serum [BARLOW *et al.*, this *Bulletin*, 1958, v. 33, 992]. COWAN [*ibid.*, 1959, v. 34, 180] cast doubt on the validity of this relationship because he found not only that different phages were neutralized by normal sera to different extents but also that the ratios of neutralization of different phages varied with different sera.

The authors have studied the T2 neutralizing activity of sera from 82 normal people, 103 patients with bacterial infections, 39 with leukaemia, 47 with lymphoma or sarcoma, 9 with multiple myeloma and 2 with paroxysmal nocturnal haemoglobinuria. They found that compared with normal sera T2 neutralizing activity was low in acute bacterial infections, rising to normal or higher in those who recovered, and serum complement behaved similarly. Phage neutralizing activity was low in serum from patients with chronic lymphocytic leukaemia, Hodgkin's disease, and advanced multiple myeloma, and it was normal or high in cases of chronic myelogenous monocytic leukaemia, less advanced multiple myeloma and most cases of reticulum cell and lymphosarcoma. Complement titres were normal or high in all these cases.

These findings agree by and large with those of others who used zymosan to assay properdin, and the authors therefore conclude that "phage neutralizing activity (PhN) of serum may reflect properdin."

Janice Taverne

COHN, Z. A. & HIRSCH, J. G. **The Isolation and Properties of the Specific Cytoplasmic Granules of Rabbit Polymorphonuclear Leucocytes.** *J. Exper. Med.* 1960, Dec. 1, v. 112, No. 6, 983–1004, 3 text figs. & 2 figs. on pl. [30 refs.]

"A method has been described for isolation of the specific cytoplasmic granules of rabbit polymorphonuclear leucocytes. Homogeneous suspensions of leucocytes were disrupted by lysis in 0.34 M sucrose. This procedure liberated the cytoplasmic contents of the cell and dissolved a considerable proportion of the nuclei. Following disruption, the sucrose lysate was separated into three fractions by differential centrifugation, *i.e.* 400 *g* or nuclear pellet, 8,200 *g* or granule pellet and the postgranule supernate. Microscopic examination revealed that the 8,200 *g* pellet was composed of intact granules as well as occasional mitochondria. The other two fractions were morphologically heterogeneous.

"Studies with isolated granules demonstrated their lysis by a variety of weak acids and surface-active agents. When buffered solutions were employed between the ranges of pH 2.0 and 9.0, granule lysis began at pH 5.5 and was complete at pH 4.0.

"Chemical analysis disclosed that the granule pellet contained protein and phospholipid with only traces of nucleic acids.

"Approximately 70 to 80 per cent of the total cellular antimicrobial agent phagocytin was present in the granule fraction. This material was liberated from the granules by acid (pH 5.0 or lower).

"Studies on selected enzymes showed that acid phosphatase, alkaline phosphatase, nucleotidase, ribonuclease, deoxyribonuclease, and beta glucuronidase were predominantly localized in the granule fraction. Approximately 50 per cent of total cellular lysozyme and cathepsin were also present in the 8,200 *g* pellet. Disruption of the granules was associated with the release of the majority of granule protein and enzymes in a non-sedimentable form. The properties and composition of rabbit polymorphonuclear leucocyte granules seem to be analogous to those of liver lysosomes."

HIRSCH, J. G. & COHN, Z. A. **Degranulation of Polymorphonuclear Leucocytes following Phagocytosis of Microorganisms.** *J. Exper. Med.* 1960, Dec. 1, v. 112, No. 6, 1005–14, 1 coloured fig. on pl.

Continuing their work on the cytoplasmic granules of polymorphonuclear leucocytes [this *Bulletin*, 1960, v. 35, 1066], the authors found that, after rabbit or human polymorphs had phagocytosed micro-organisms, there was a marked reduction in the number of granules in the cells; this reduction occurred quite rapidly (within 30 mintues after the addition of washed bacteria to leucocytes made adherent to a glass slide by a new sedimentation technique), and was directly related to the quantity of bacterial matter engulfed. The organisms used included *Bacillus subtilis*, *Salmonella typhi-murium*, a Group A *Streptococcus* and *Mycobacterium smegmatis*. Zymosan, the preparation from yeast cell wall, acted similarly.

The authors conjecture that when the foreign particles enter the phagocyte, glycolysis is accelerated, acid is produced, the *p*H falls, and the polymorph's granules are lysed, releasing their phagocytin and digestive enzymes. It is not yet clear whether the granules discharge their phagocytin into the cytoplasm of the leucocyte or into phagocytic vacuoles around the engulfed material.

D. A. Cannon

COHN, Z. A. & HIRSCH, J. G. **The Influence of Phagocytosis on the Intracellular Distribution of Granule-Associated Components of Polymorphonuclear Leucocytes.** *J. Exper. Med.* 1960, Dec. 1, v. 112, No. 6, 1015–22, 2 figs.

As a result of the work described in the previous paper [see above], the authors investigated the fate of the phagocytin and a number of hydrolytic enzymes released from the granules of rabbit polymorphonuclear leucocytes which had phagocytosed heat-killed bacteria. Comparisons were made of the properties of two leucocyte populations, one of which was actively ingesting a large number of heat-killed *E. coli* or *B. subtilis*. Following the uptake of the bacteria, there was a striking reduction in the phagocytin recoverable from the leucocytes: it seemed that the phagocytin, once released from

the granules, was "consumed" upon exposure to the ingested bacteria. On the other hand, although there was a progressive loss of the hydrolytic enzymes (the phosphatases, beta-glucuronidase and cathepsin) from the cytoplasmic particles, there was no significant difference in the total enzyme activities of the control and phagocytosing leucocytes, indicating that phagocytosis resulted primarily in an intracellular redistribution of these components. These findings are consistent with the lysis of granules following phagocytosis and the liberation of granule constituents into the cytoplasm of the leucocyte.

D. A. Cannon

MELLY, Marian A., THOMISON, J. B. & ROGERS, D. E. **Fate of Staphylococci within Human Leukocytes.** *J. Exper. Med.* 1960, Dec. 1, v. 112, No. 6, 1121–30, 2 text figs. & 20 figs. on 2 pls. [14 refs.]

Using a Zeiss photomicroscope, with phase contrast lighting and an interference filter, the authors observed (and have produced good pictures of) the phagocytosis of staphylococci by human polymorphonuclear leucocytes in a slide phagocytic system which incorporated a method of disrupting the leucocytes by an electrical shock. Pathogenic staphylococci survived long periods of time within living phagocytes, whereas non-pathogenic staphylococci were rapidly destroyed. This intracellular survival could not definitely be related to leucocyte damage, although cells in which staphylococci survived often seemed less vigorous than cells which killed ingested cocci. Both pathogenic and non-pathogenic cocci were seen to divide within living leucocytes: occasionally pathogenic staphylococci multiplied in dying cells after long periods of intracellular residence. Phagocytosis of more than one pair of staphylococci by a single leucocyte appeared to act as a stimulus to bacterial destruction. Multiple ingesting of pathogenic staphylococci reduced the incidence of survival of the total microbial population contained within the cell. It is suggested that such multiple ingestions may provoke more extensive lysis of granules and release of intracellular enzymes to the cytoplasm of the leucocyte [see COHN and HIRSCH, above].

D. A. Cannon

WERTMAN, K. F. & SYPHERD, P. S. **The Effects of Riboflavin Deficiency on Phagocytosis and Susceptibility to Infection.** *J. Immunology.* 1960, Nov., v. 85, No. 5, 511–15. [12 refs.]

When male white rats were fed on a diet deficient in riboflavin their leucocytes showed a marked deficiency of phagocytic activity against pneumococci. Compared with inanition controls, *ad libitum* controls, and animals whose deficient diet was subsequently supplemented with riboflavin, the test animals were clearly more susceptible to challenge by intraperitoneal injection with 2 ml. of a 24-hour broth culture containing 2×10^5 virulent type-1 pneumococci per cmm. 20 of 20 *ad libitum* controls survived the challenge, compared with 20 of 30 inanition controls, 5 of 30 riboflavin-deficient rats, and 20 of 22 riboflavin-deficient rats given a riboflavin supplement of 60 μgm. daily for 1 week before challenge after 7 weeks of deficiency. The results of the phagocytic experiments were equally clear and in the same direction.

[This experimental model appears to have given very clear results and the experiments are fully controlled in all necessary respects.] *J. W. Howie*

HACKETT, E. & BEECH, Margaret. **Transient Appearance of "Autoimmune" Antibodies during Prophylactic Immunization.** *J. Immunology.* 1960, Nov., v. 85, No. 5, 533–8, 1 fig.

The "autoimmune complement fixation" (AICF) reaction described by GAJDUSEK (*Nature*, 1957, v. 179, 666; *Arch. Intern. Med.*, 1958, v. 101, 9) has been observed in various conditions and also in normal subjects. The authors obtained a transient positive reaction in 2 out of 7 girls, aged 18–21 years, who were being actively immunized against poliomyelitis, tetanus, typhoid and paratyphoid fevers. One girl reacted with all 5 antigens used in the test (adrenal, liver, kidney, thyroid and lung), the other only with kidney. (A third girl reacted with all the antigens except thyroid, but at unchanging titres both before immunization and throughout the investigation.)

Several possible explanations are suggested: (a) a classical immune response; (b) an anamnestic response; (c) increased gamma-globulin activity; (d) a subclinical viral infection; (e) the result of a temporary proliferation of one of BURNET'S "forbidden clones" of antibody-forming cells [this *Bulletin*, 1960, v. 35, 208], which temporarily escaped the homeostatic mechanism. Reasons are given for favouring the last explanation: in both girls it seemed that Burnet's homeostatic mechanism was constitutionally weak.

D. A. Cannon

Book Reviews

BAADER, Ernst W. **Klinische Grundlagen der sechsundvierzig meldeplichtigen Berufskrankheiten.** [The Clinical Basis of the 46 Notifiable Occupational Diseases] 5th Edition. pp. xii + 479, 69 figs. & 12 coloured pls. 1960. Berlin. München 15: Urban & Schwarzenberg, Pettenkoferstrasse 18, Germany. [DM 58.]

In his preface the author states that he limits himself to the 46 notifiable and compensatable diseases of occupation in the 3 German states (Bundesrepublik, D.D.R., Saarland) and Austria, and to some non-notifiable diseases, in which the differential diagnosis is discussed. What we have here, however, is a very comprehensive account of industrial disease compressed into the 479 pages of a book of handy size.

As we turn over the pages we are struck by the lack of paragraphing, so different from the conspicuous and helpful paragraphing of the English counterpart of the book—Hunter's *Diseases of Occupations*. This may make it a little more difficult to look up a particular point, but it certainly saves space. Considering the range of subjects, the illustrations are relatively few, but they are all to the point. The coloured plates are very good, especially those illustrating mercury poisoning.

The greater part of the book is devoted to clinical findings. The account of each disease begins with a description of the obnoxious material or activity and the processes in which it occurs. At the conclusion, the prognosis, the treatment and preventive measures are separately discussed. Lastly, the permissible limit of concentration at the working place of the poison or dust is given as a working guide to the limits of danger.

In an early chapter the author gives reasons for doubting the value of the present standards. He awaits publication of permissible limits agreed on at the Prague conference of 1959 but meanwhile he advises doctors to avoid looking on biology as mathematics.

The list of 46 notifiable diseases in the 6th Regulation of the Bundesrepublik was not in force at the time of the publication of this book but its ratification was imminent. The diseases on the list reflect German experience in the same way as the British list—National Insurance (Industrial Injuries) (Prescribed Diseases) Regulations, 1959, Part I, First Schedule; Statutory Instruments 1959, No. 467—reflects ours. The most important diseases are common to both lists, the German one being more extensive in its coverage.

As both lists are headed by lead or its compounds, we may take Baader's description of this classical industrial disease as typical of the remainder of the book. The subject is dealt with very fully and in a practical fashion in 28 pages. The sources of lead poisoning are given in detail with a warning that in many trades lead compounds are only occasionally used, so that the risk is increased because no one realizes the danger.

The modes of entry, the storage of lead in the body and its elimination are given full consideration. The author frequently draws from his own experience and in connexion with the estimation of lead in the stools, mentions a fraudulent claim where the claimant had 161·9 mgm. lead in his stools. He had been enjoying the highest compensation for industrial disease.

The author considers that over 4 mgm. lead in 100 gm. stool 4 weeks after the end of lead exposure is a proof of deliberate self-poisoning. The cardinal symptoms are anaemia, the lead line, punctate basophilia and the presence of coprophyrin III in the urine. Methods of demonstrating coprophyrin in the urine with the spectroscope and ultraviolet light are given full attention. All the other symptoms with their differential diagnosis are completely presented: there is also a note on the changes in the sexual organs. In discussing prevention the author expresses the opinion that milk is good nourishment, but it has no specific action against lead. To repeat the criticism about paragraphing, the section on tetraethyl lead is rather lost in the general review of lead poisoning, and its description seems rather curtailed as a result.

The remainder of the poisons are equally well treated so that only a few points need be mentioned. Chronic carbon monoxide poisoning is said to occur when subtoxic doses of the gas are inhaled; but on account of the vagueness of the symptoms it is not so frequently recognized as the acute type.

Disturbances of sight and hearing are particularly mentioned as symptoms; there are disturbances of balance, leading to a characteristic gait, which is illustrated by 4 shots of a film. Psychological symptoms, often mistaken for hysteria, are also present.

The condition resulting from the use of vibrating tools is a compensatable disease in Germany and at present is the fourth most common industrial disease there. The disease is compared with silicosis in that it may appear years after the exposure has ceased and may then progress. The dust diseases are all given very full attention. Silica, talc, aluminium, as causes of fibrosis of the lungs, present the author with material of which he has taken full advantage. The same holds good for asbestos, but there is no mention of possible alveolar capillary block, the recognition of which may be a factor in diagnosis. Incidentally asbestosis in combination with lung cancer is a compensatable disease in Germany.

The section devoted to non-pneumoconiotic industrial diseases of the lung, that is, byssinosis, farmer's lung, etc., starts with the bronchitis which develops in persons exposed to dust. In the Ruhr coalfields, bronchitis and emphysema without or with minimal silicosis is 3 or 4 times as common as in non-miners and is a greater cause of invalidism than silicosis. It arises independently of silicosis and may in fact prevent the development of a silicotic fibrosis.

Chronic bronchitis from work in dusty trades is not a compensatable condition; in old people with no dust exposure it is very common.

The author's views are shown by the statement that it is not the intention of the book to plead for compensation but to spread medical knowledge and to prevent senseless curtailment of life. He then quotes CARSTENS (*Probleme der Pneumokoniosen, Sammlung Arbeitsmedizin*, Heft 33, Leipzig, 1960, Verlag Barth) that with a timely change of job many would remain capable of work for years and avoid with certainty an agonizing

death from respiratory insufficiency as a result of prolonged occupational injury.

This is an excellent textbook for doctors in Germany interested in industrial diseases. The references at the end of each section will in themselves provide a mine of information to those inside or outside Germany pursuing a particular subject. The book itself will provide help to those outside Germany, since it covers the ground completely. *Charles L. Sutherland*

GUNSALUS, I. C. & STANIER, Roger Y. [Edited by.] **The Bacteria. A Treatise on Structure and Function. Vol. I: Structure.** pp. xiv + 513, illustrated. 1960. New York 3: Academic Press Inc., 111 Fifth Avenue, N.Y. London: 17 Old Queen Street, S.W.1. [$13.00.]

This book constitutes the first of 5 volumes to be published under the general title of *The Bacteria.* Metabolism, biosynthesis, growth and heredity will be the subjects of the remaining volumes, this first volume being concerned with the structure of the bacterial cell. The editors in their preface state that "Heretofore, there has been no comprehensive source of information about modern knowledge of the general biological properties of bacteria" and express the hope that this treatise will help to fill the gap. To this end they have enlisted the aid of an imposing array of contributors, each an accepted authority on his subject, and the completed work should provide a concise and well documented statement of general bacteriological knowledge at the present time—a valuable source book for the immediate future and a no less valuable point of orientation for workers in years to come.

Volume I contains 10 chapters dealing both with the details of cell structure and with the techniques used in their investigation. S. E. LURIA writes on the composition and organization of bacterial protoplasm, R. G. E. MURRAY on the internal structure of the cell, M. R. J. SALTON on the surface layers of the cell, C. WEIBULL on movement, C. F. ROBINOW on the morphology, development and germination of bacterial spores, K. MCQUILLEN on bacterial protoplasts, E. KLIENEBERGER-NOBEL on L-forms, T. F. ANDERSON on bacterial viruses, E. S. LENNOX on the antigenic analysis of cell structure and A. G. MARR on the localization of enzymes in bacteria.

Each chapter is authoritative, yet reasonably concise and the excellent system of sub-heading used throughout the book adds much to its readability and to the ease of locating information. The whole presents a pattern of excellence in which it is difficult to single out particular sections as especially deserving of commendation. Bibliographies are extensive without becoming unwieldy, providing admirable introductions to the specialized literature. There are occasional lapses in uniformity of nomenclature—"*Bacillus proteus*" and "*Proteus vulgaris*" should not occur randomly mixed in the same chapter—and authors are not always in agreement when assessing particular data. This is hardly surprising. Much in this field is still controversial and the editors are wise to allow their contributors a free hand in such matters.

It is perhaps hard to criticize a book of this size on grounds of incompleteness but such a criticism must be made. In a volume of this kind we might have expected at least one chapter devoted to the lesser known bacterial forms; instead we are left with a few brief references or, more often than not, with nothing at all. Is it not time that we admitted the presence of resistant cysts in *Sporocytophaga* and *Azotobacter* and accorded them the attention they deserve? Why do the iron bacteria merit only half a sentence in the whole book? What is it about the structurally fascinating Chlamydobacteriales, the Myxobacteriales and many other forms that sends the contributors scurrying for safety behind the protective skirts of the rods and cocci beloved of the "classical" bacteriologist? This curtailment of the scope of the volume certainly does not arise from a lack of published observations or from an absence of able authors. It ought not to arise from doubts as to the value of a coherent discussion of the more unusual bacterial forms. The volume as it stands should perhaps be entitled "Some of the Bacteria"—an eager public awaits the appearance of "The Rest".

This volume is extensively illustrated and is produced with the great care and high quality normally associated with Academic Press. As a discourse on bacterial structure it demands a place on the shelves of every serious microbiologist and in every teaching library. As a balanced account of bacterial anatomy it must be accused of bias towards a too conservative view of the scope of its subject. This is a pity since it has reduced to the level of an excellent textbook what could so easily have been an invaluable milestone in the bacteriological literature. *John R. Norris*

CIBA FOUNDATION [WOLSTENHOLME, G. E. W. (O.B.E., M.A., M.B., M.R.C.P.) & O'CONNOR, Maeve (B.A.), Editors]. **Cellular Aspects of Immunity.** pp. xii + 495, numerous figs. 1960. London: J. & A. Churchill Ltd., 104, Gloucester Place, W.1. [60s.]

In its 10th Anniversary year the Ciba Foundation is to be congratulated on arranging in this Symposium such an inspiring list of speakers, and such an interesting collection of papers, on the Cellular Aspects of Immunity. The opening papers deal with the cells themselves: after a short introduction by A. FAGRAEUS on the nomenclature of immunologically competent cells, R. ROBINEAUX and J. PINET describe an *in vitro* study of some mechanisms of antigen uptake by cells, illustrated by time-lapse phase contrast, interference microcinematographic films and fluorescence microphotographs; and C. LAPRESLE and T. WEBB discuss the degradation of protein antigens by intracellular enzymes. Fine microcinematographic studies of the plasma cells by J. P. THIÉRY are followed by excellent electron microscopy, by W. BERNHARD and N. GRANBOULAN, of recticular cells, lymphocytes and the plasma cell line. M. SIMONSEN deals with the identification of immunologically competent cells.

Next come the theories: P. B. MEDAWAR on immunological tolerance and F. M. BURNET and J. LEDERBERG on the clonal selection theory of antibody formation. Both concise dispositions are followed by illuminating discussions by experts in this academic field. Thence to experimental work: T. N. HARRIS and Susanna HARRIS

describe lymph node cell transfer in relation to antibody formation; P. GRABAR and P. CORVAZIER study the formation of antibodies *in vitro*; and P. BURTIN discusses the cellular origin and immunological importance of the serum proteins, mainly the gamma globulins.

After a theoretical discussion by D. W. DRESSER and N. A. MITCHISON on the cellular basis for the immunological memory, comes a summary by H. S. LAWRENCE of the biological and immunological properties of transfer factor. A comprehensive paper by B. H. WAKSMAN on a comparative histopathological study of delayed hypersensitive reactions leads on to a discussion by P. A. GORER of the interactions between sessile and humoral antibodies in homograft reactions. A more clinical approach is reached in the paper by R. T. SMITH on the response to active immunization of human infants during the neonatal period.

In another experimental direction G. A. VOISIN and F. TOULLET demonstrate modifications of capillary permeability in immunological reactions mediated through cells. Taking one of the forms of hypersensitivity, the anaphylactic reaction, B. N. HALPERN, P. LIACOPOULOS, R. BINAGHI and R. LIACOPOLOS-BRIOT study the patterns and mechanisms of fixation of anaphylactic antibody on living tissues *in vitro*. After H. G. KUNKEL, H. R. HOLMAN and H. R. G. DEICHER have discussed multiple "autoantibodies" to cell constituents in systemic lupus erythematosus, P. MIESCHER, N. S. COOPER and D. HUREZ report on the *in vitro* action of antigen-antibody complexes on thrombocytes and erythrocytes.

F. M. BURNET leads off the final group discussion which attempts, obviously without much hope of complete success, to summarize the papers read at what must have been a very packed three days; and yet what an illuminating discussion this turns out to be.

This is a volume of the greatest interest to immunologists, no matter to which "school" they belong, because it is a compendium of immunological facts and theories, excellently compiled and edited which will serve for long as a stimulus to further thought and work on these aspects of immunity. *D. A. Cannon*

ELLIS, R. W. B. **Health in Childhood.** 251 pp. 16 figs. & 16 pls. Pelican Books A496. 1960. Harmondsworth: Penguin Books, Ltd., Middlesex. [5s.]

This book has been written for "the man in the street," but it is difficult to believe that such a man will find it very helpful as the book is essentially an introduction to the study of health and disease in children. Starting with a survey of the social environment of the child, Professor Ellis goes on to discuss genetic make-up, immunity and allergy and then considers various selected disease syndromes. In the third chapter the author discusses those factors that can affect a child during its intra-uterine life, in chapter 4 the hazards of birth and in chapter 5 the newborn infant. The last three chapters of the book are devoted to nutrition and feeding, growth and development and the handicapped child. The information given in the book, as one would expect from the author, is sound and interesting, but much of it is not of practical importance to parents. For general-trained nurses, children's officers and other professional workers desirous of understanding the causation of illness in children, this book will be of value.

M. D. Warren

KRUGMAN, Saul [M.D.] & WARD, Robert [M.D.]. **Infectious Diseases of Children.** 2nd Edition. 398 pp., 55 figs. & 7 pls. (1 folding). 1960. St. Louis: The C. V. Mosby Co. London: Henry Kimpton, 134, Great Portland Street, W.1. [97s. 6d.]

Two paediatricians, one in New York and one in Los Angeles, combined to produce this book in 1958, and the second edition has appeared within the short space of two years. The chief reason given for this short interval between the editions is the recent rapid accumulation of knowledge of viruses and of the human diseases caused by them.

A new chapter on acute respiratory infections sets out briefly the known roles of the 40 or more viruses now established as aetiological agents in these illnesses. Similarly, the enteroviral infections including poliomyelitis and Coxsackie illnesses have been grouped together, and a new section added on the ECHO sub-group and its associated syndromes. An appraisal of the promising new attenuated oral vaccines for poliomyelitis is included. New information is given on the adenoviruses, infectious hepatitis, herpetic infections, measles virus, rubella during pregnancy, and chickenpox pneumonia (which, however, occurs almost always in adults). The management of acute bacterial meningitis, and of staphylococcal infections, has been rewritten, but in the sort of catalogue form common to the whole book, with insufficient practical detail of the management of patients. Tuberculous meningitis is disposed of in a few lines. There is a new chapter on rabies which is fuller, especially on prevention and treatment. The treatment of respiratory poliomyelitis occupies only a few lines, and the use of the respirator in severe tetanus and drugs like chlorpromazine are not even mentioned. Evidently the authors have little or no practical experience of these procedures, or of methods of control of communicable diseases within the hospital—a subject dealt with by M. GREENBERG, who, however, is in favour of the treatment of typhoid carriers in a *general* ward. Other subjects not included are gastro-enteritis of infants, tuberculosis, syphilis, leptospirosis, yellow fever, malaria, and fungal diseases.

The book must be rated more highly on the scientific than on the practical level. Its defects stem from the deficiences in the training and experience of paediatricians in infectious diseases—no experience with adolescents and adults, and little experience in the practical management of infectious diseases in the mass. The balance of the book suffers accordingly, and the practical care of the patient is subordinated to theory. It is perhaps significant that all the colour plates and nearly all the illustrations are borrowed from other sources. In another sense also the book is askew; there is hardly a reference to European literature. *H. Stanley Banks*

KERVRAN, Roger [M.D.] **Laennec—His Life and Times.** [Translated from the French by D. C. ABRAHAMS-CURIEL.] pp. x + 213. 1960. London. New York. Paris. Oxford: Pergamon Press, Ltd., Headington Hill Hall. [21s.]

Every doctor has heard of Laennec, and vaguely of his association with the discovery of the principle of auscultation by means of an instrument. Direct auscultation, in which the physician applies his ear directly to the chest of the patient, had long been known for the investigation of heart disease, though it was not extensively practised, but it is an awkward procedure, and Laennec, confronted with a patient in whom direct auscultation was regarded as unsuitable, remembered a well-known phenomenon of acoustics—"if the ear is applied to one end of a beam, a pin prick is most distinctly heard at the other end." He rolled sheets of paper tightly into a tube, and applied one end to the chest, and his ear to the other, with most gratifying results. The stethoscope was born, and Laennec went on to use it not only for heart sounds but also for breath sounds; it was a great advance.

But of course this was not a mere single episode; it was the reflection of an active mind working in a period of intellectual activity and unrest. The author of this book tells very completely the story of Laennec's life from his childhood in Brittany where he was born in 1781, through his early studies in the classical languages and French literature, to his move to Paris, and finally to his return to Brittany and his death there at the early age of 45. He lived through the French Revolution, and was caught up in it, seeing in his youth some of the excesses perpetrated in its name. He also lived through the Napoleonic era, but seems not to have been closely involved except in the campaign of 1814, when his Paris wards were full of wounded and sick soldiers, typhus being prominent. His interests were professional and artistic, and as a result of his discovery of auscultation he was led to pursue his analysis of sounds heard through his instruments, in finer and finer detail, and to relate them to the pathological conditions in the organs beneath; he was the first to recognize and describe bronchiectasis and emphysema. The investigation he undertook was in the great tradition of observation and interpretation, it was new and accurate, and it was immensely important for medicine as a whole.

Apart from a few mis-spellings such as Avenbrugger and Halnemann (p. 133) the book is well printed and produced, and both author and translator are to be congratulated on an important historical work.

Charles Wilcocks

We record with deep regret the death on 6th April, 1961 of Sir William George Savage, M.D., B.Sc., D.P.H., who had been a regular contributor to this *Bulletin* from 1926 (Volume 1) to 1960.

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